Introduction: Analysis of Data Derived from Medical Images

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Outline

- Snippets of examples of medical imaging data
- 3 main analysis techniques:
  - Detection
  - Estimation
  - Classification / learning

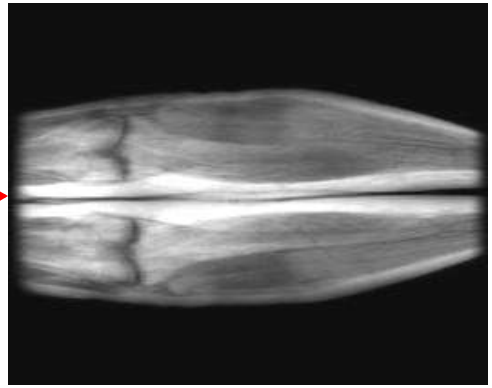
Detection Problems

- edge detection
- arrythmia detection in AED
- detection of onset of Alzheimer's
- epileptic episode
- Detection of tumor in mammography exams
- Detection of fatty tissue from abdominal CT exam

Estimation Problems

- Given instrument data plus noise and artifacts, estimate quantity of interest

.... 0 1 1 0 1 0 1 0 1....



- Reconstruction of images from raw scanner data
- Recon of brain fiber shapes from brain diffusion MRI
- Estimation of dipole relaxation properties of various tissue types from MRI
- Heartbeat estimation from ECG

Classification / learning Problems

- Patient level (e.g. patient is suffering from Alzheimer's, Parkinsons, epilepsy or healthy?)
- Organ or tissue level (e.g. texture and shape of liver – cirrhosis, carcinoma or normal?)
- Voxel level (e.g. voxel belongs to healthy tissue, malignant or benign tumor?)
- Classification of time-profiles (e.g. contrast uptake of veins vs arteries, of malignant vs benign tumors, brain atrophy of normal aging vs Alzheimer's)
- Image segmentation is voxel level classification
- Network level (of networks derived from imaging data)

Part I : Detection Problems in Medicine

What is Detection

- Deciding whether, and when, an event occurs
- Presence/absence of
  - signal
  - activation (fMRI)
  - foreground/background
  - tissue – WM/GM/CSF (segmentation)
- Measures whether statistically significant change has occurred or not

Detection

- “Spot the Money”

Matched Filters

- If the profile of a certain signal is known, it can be detected using the Matched Filter
- If the question is not IF but WHERE…
- Maximum of MF output denotes the most likely location of the object h(t)

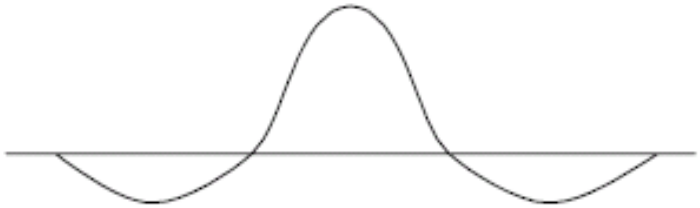
Matched Filters

- Example 1: activation in fMRI
  - Need profile model: hemodynamic response function
- Example 2: Detecting malignant tumours in mammograms
  - need profile model: temporal response to contrast agent
- Example 3: Edge detection
- Example 4: detecting contrast arrival in CE-MRA
- In each case need a model to "match" the signal

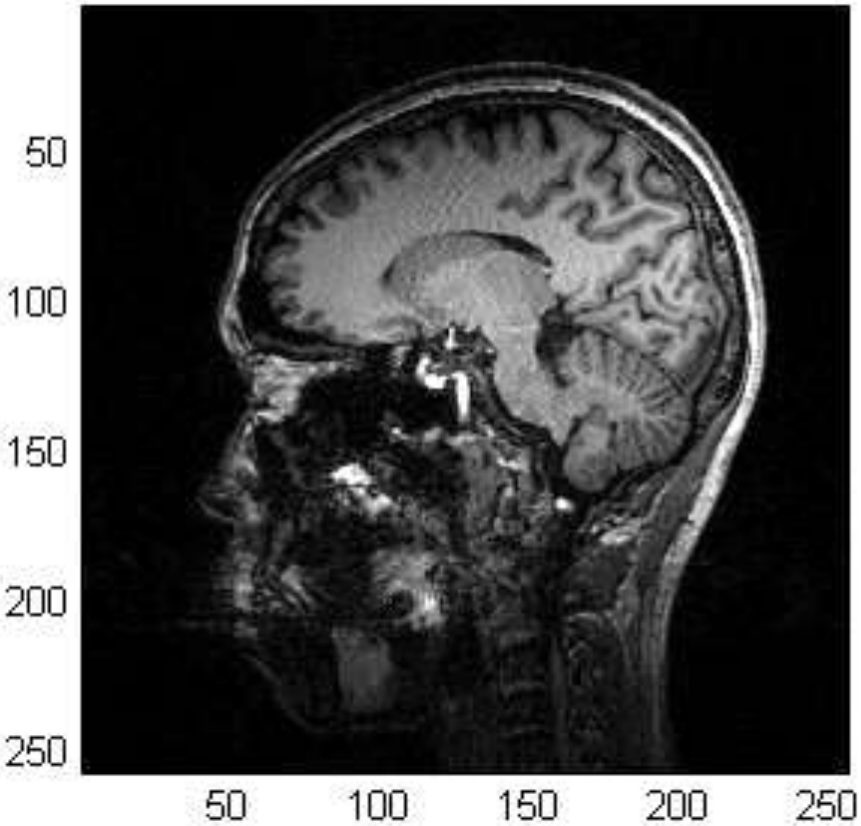
Edge Detection

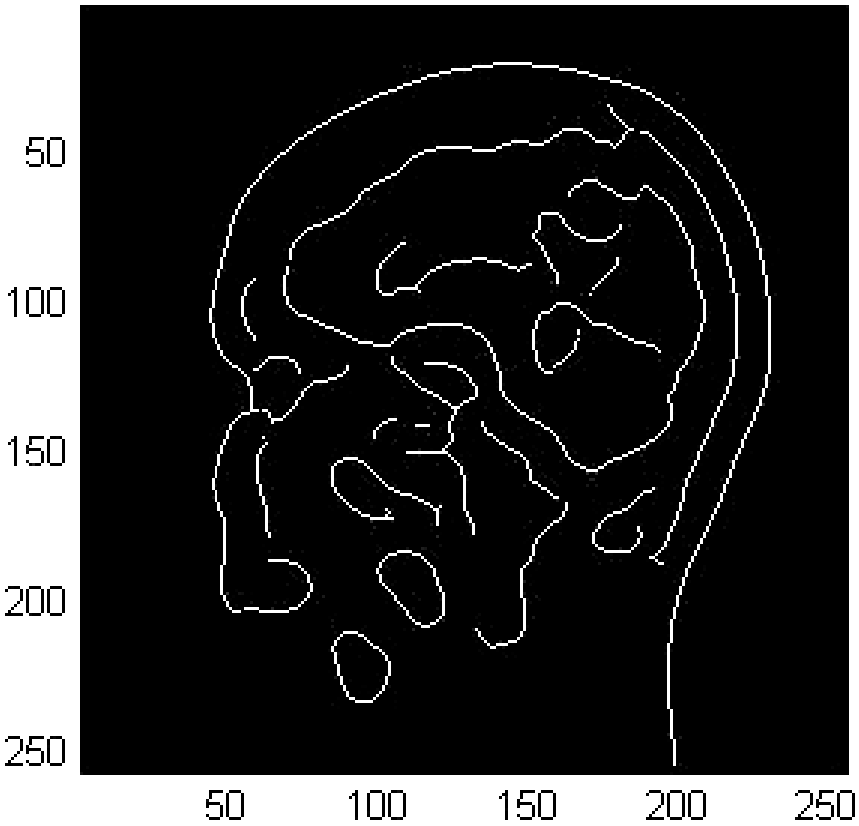
	1	
1	-4	1
	1	

$$\nabla^2(G_\sigma \star I) \; .$$



Edge Detection example using MATLAB





bw = edge(I, 'canny', sigma);

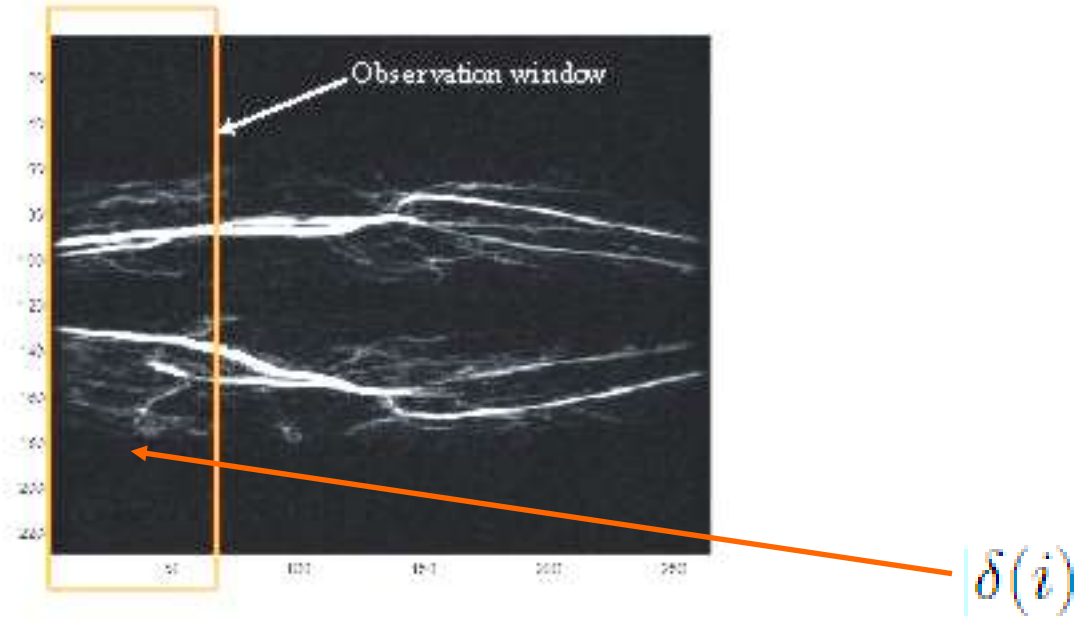
Automatic Detection of Contrast Arrival in MR Angiography

- MRA relies on good estimate of contrast arrival
- Completely unsupervised, reliable automatic method
- >90% accuracy, c.f. earlier reported method (~60% accuracy)

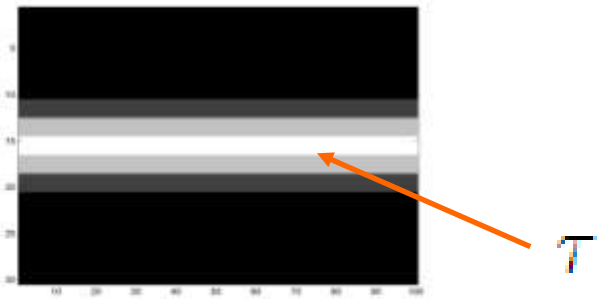
  matched filter - spatial metric

  keyhole - frequency metric

Vasculature strongly oriented horizontally

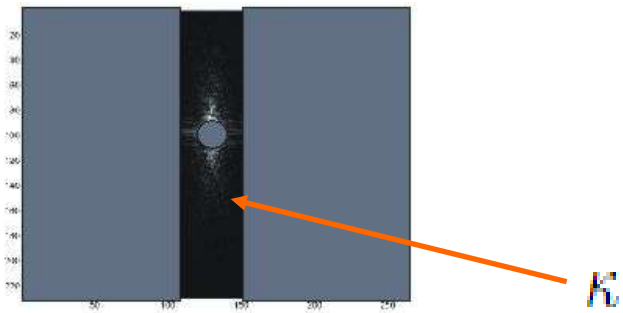


Matched Filter



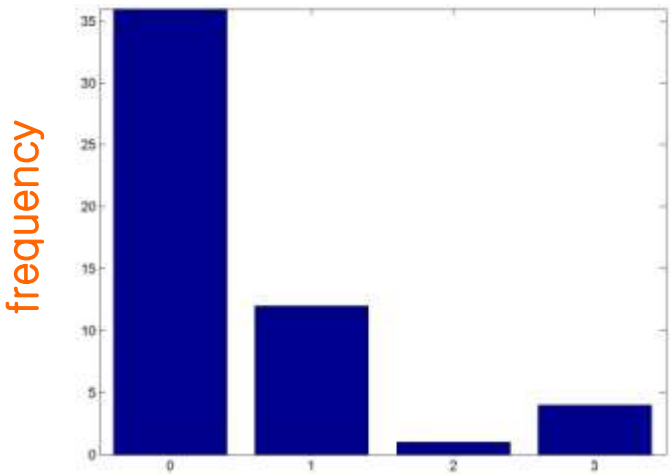
$$\lambda_{MF}(i) = \frac{||\delta(i) * *\tau||}{||\tau|| \cdot ||\delta(i)||},$$

Keyhole



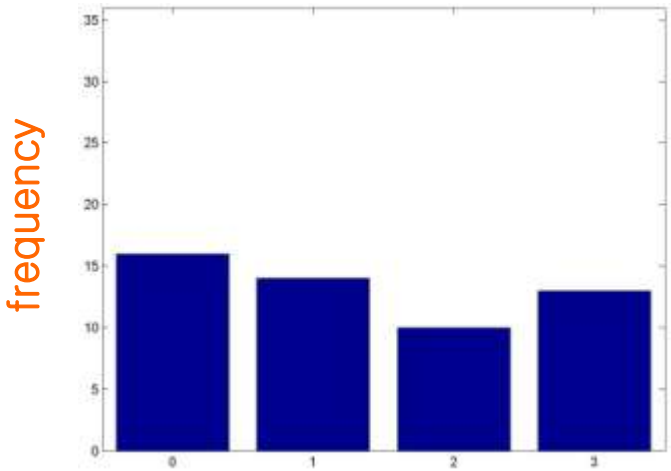
$$\lambda_{KH}(i) = \frac{||\delta_K(i) \cdot \kappa||}{||\delta_K(i)||}.$$

Results : Our method



accurate ------→ inaccurate

Earlier method

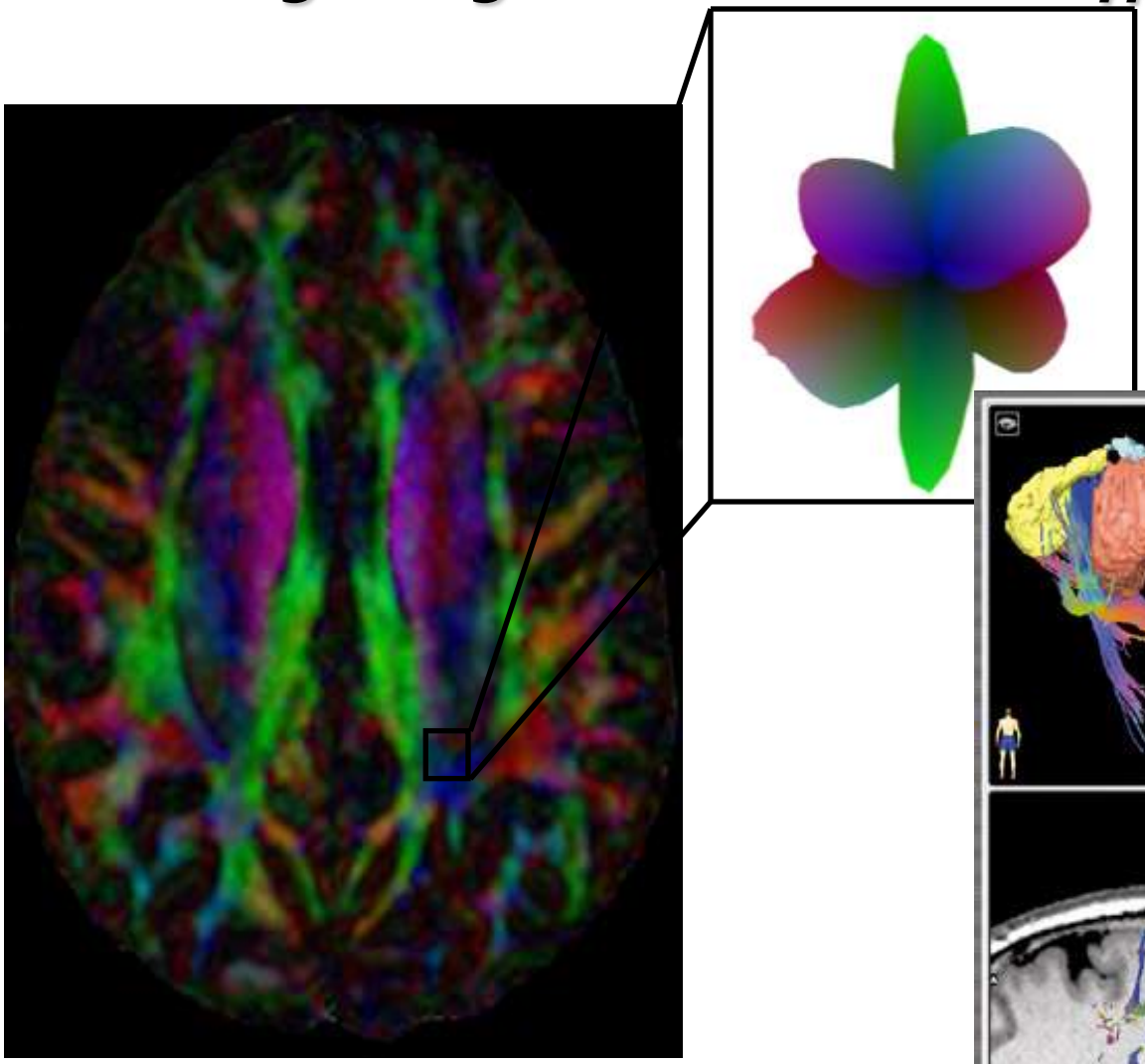


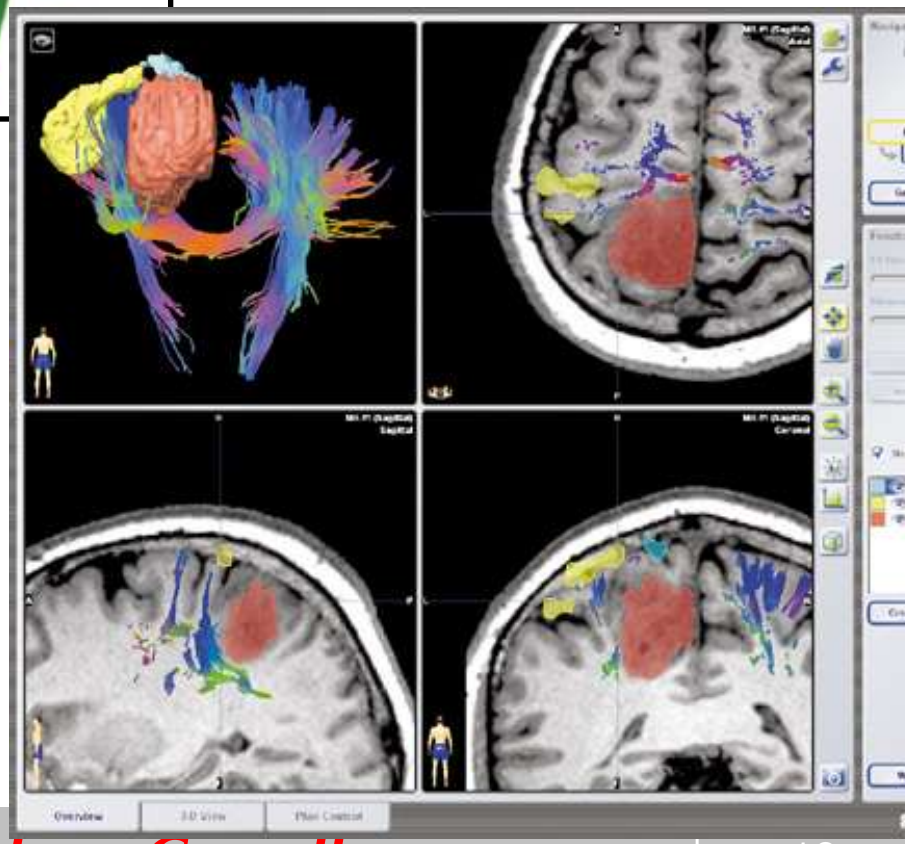
accurate ------→ inaccurate

Part II : Estimation Examples

- Estimating shapes of brain white matter fibers
- Reconstructing images from raw MRI scanner data

High Angular Resolution Diffusion Imaging





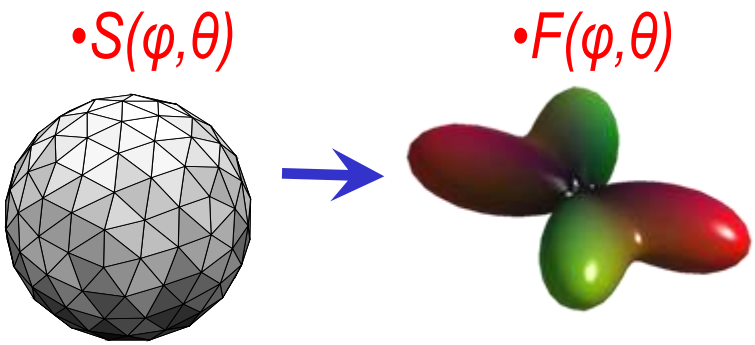
MR Diffusion Imaging

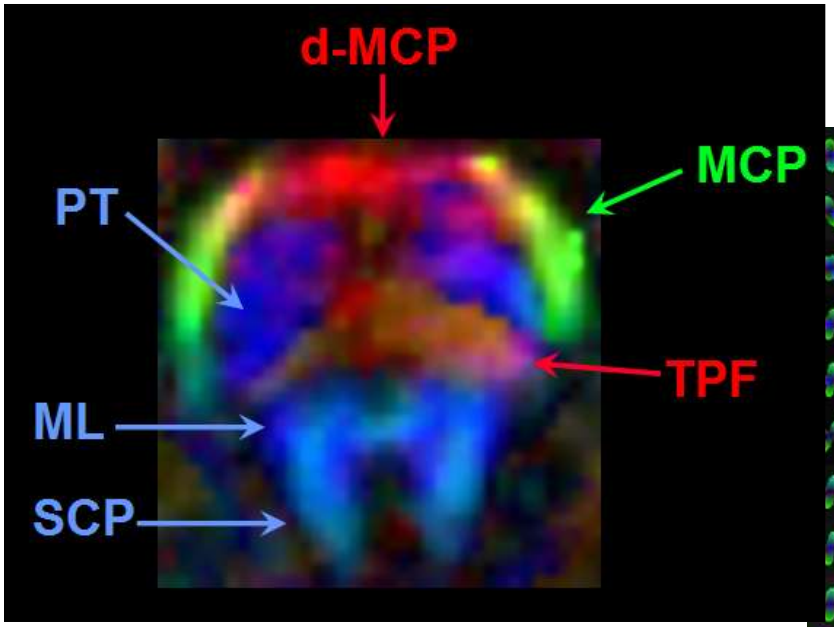
- Diffusion MRI has revolutionized in vivo imaging of brain
- Measures the directionally varying diffusion properties of water in tissue
- Anisotropy of diffusion is an important marker of extant fiber organization
- Enables probing of fiber connectivity in the brain, through tractography
- D-MRI involves taking several directional diffusion imaging measurements
- Then we fit a 3D shape to these measurements

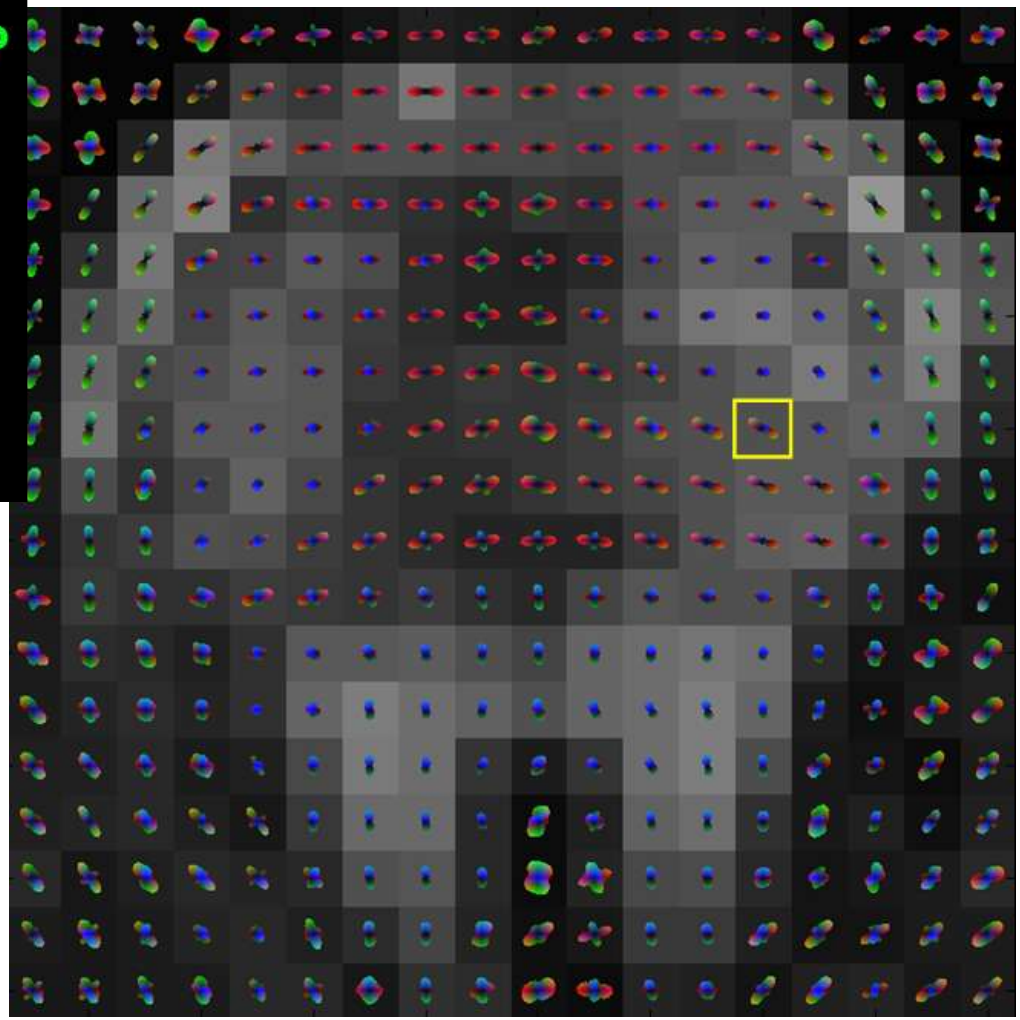
Reconstruction Problem

Basic Approach

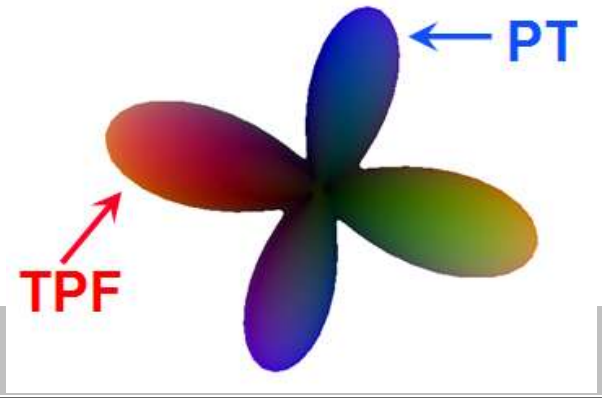
Construct a function on the unit sphere that characterizes the angular structure of diffusion anisotropy in each voxel.







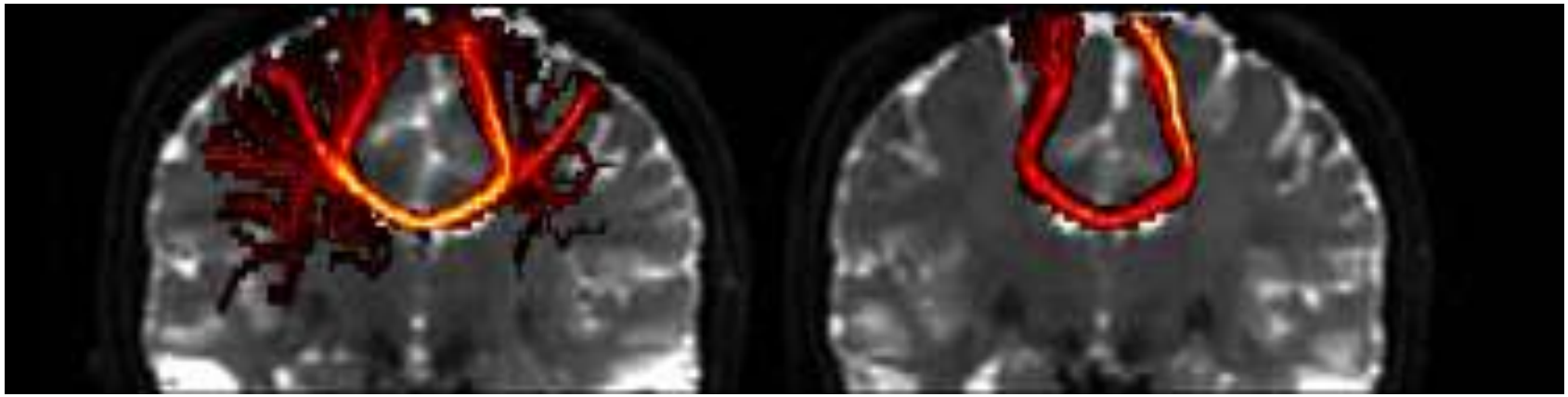
- Middle cerebellar peduncle (MCP)
- Superior cerebellar peduncle (SCP)
- Pyramidal tract (PT)
- Trans pontocerebellar fibers (TPF)



Hess CP, Mukherjee P, Han ET, Xu D, Vigneron DB
Magn Reson Med 2006; 56:104-117

Clinically Feasible HARDI Tractography

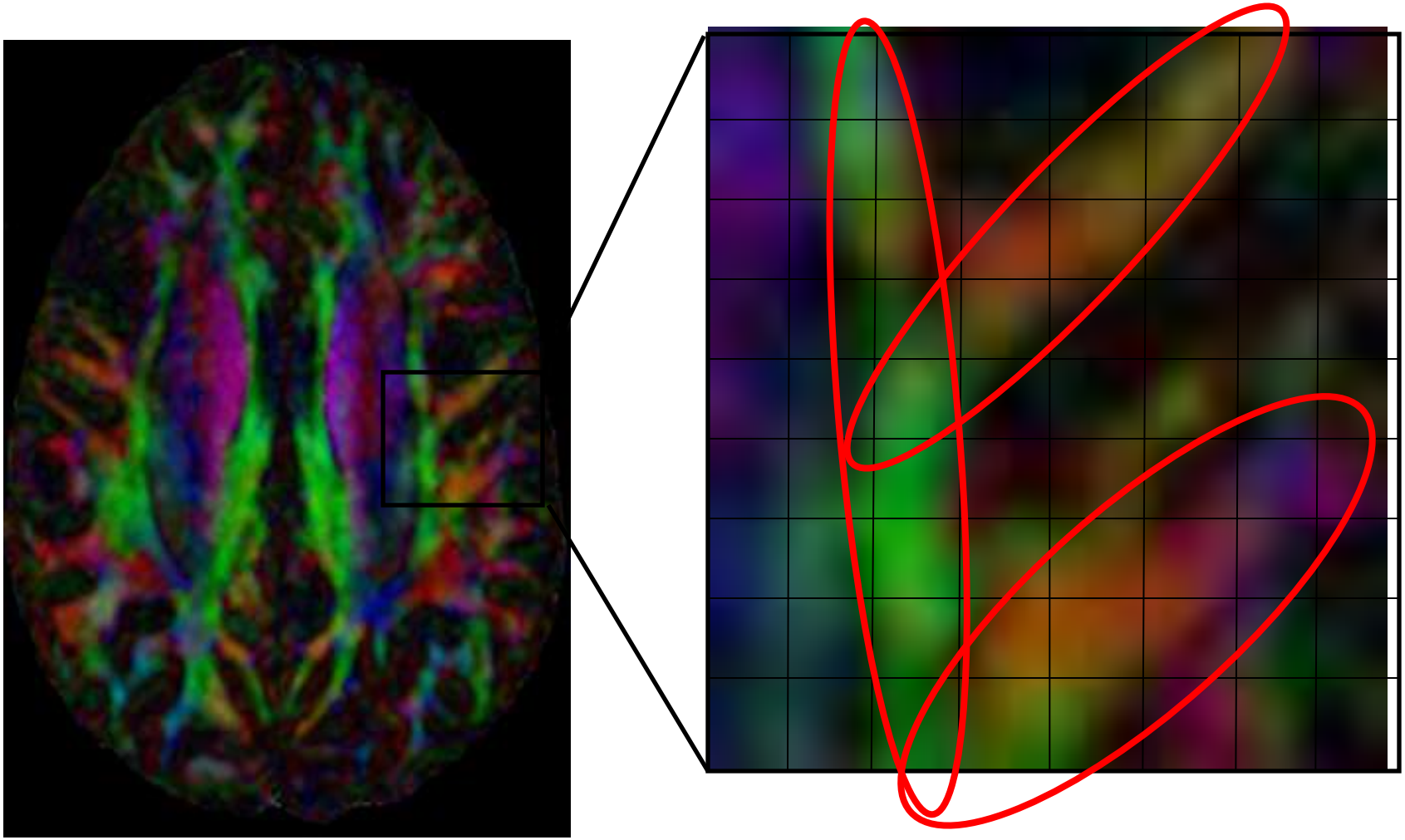
- Reconstruction quality depends on algorithm used



Harmonic *q*-ball DTI

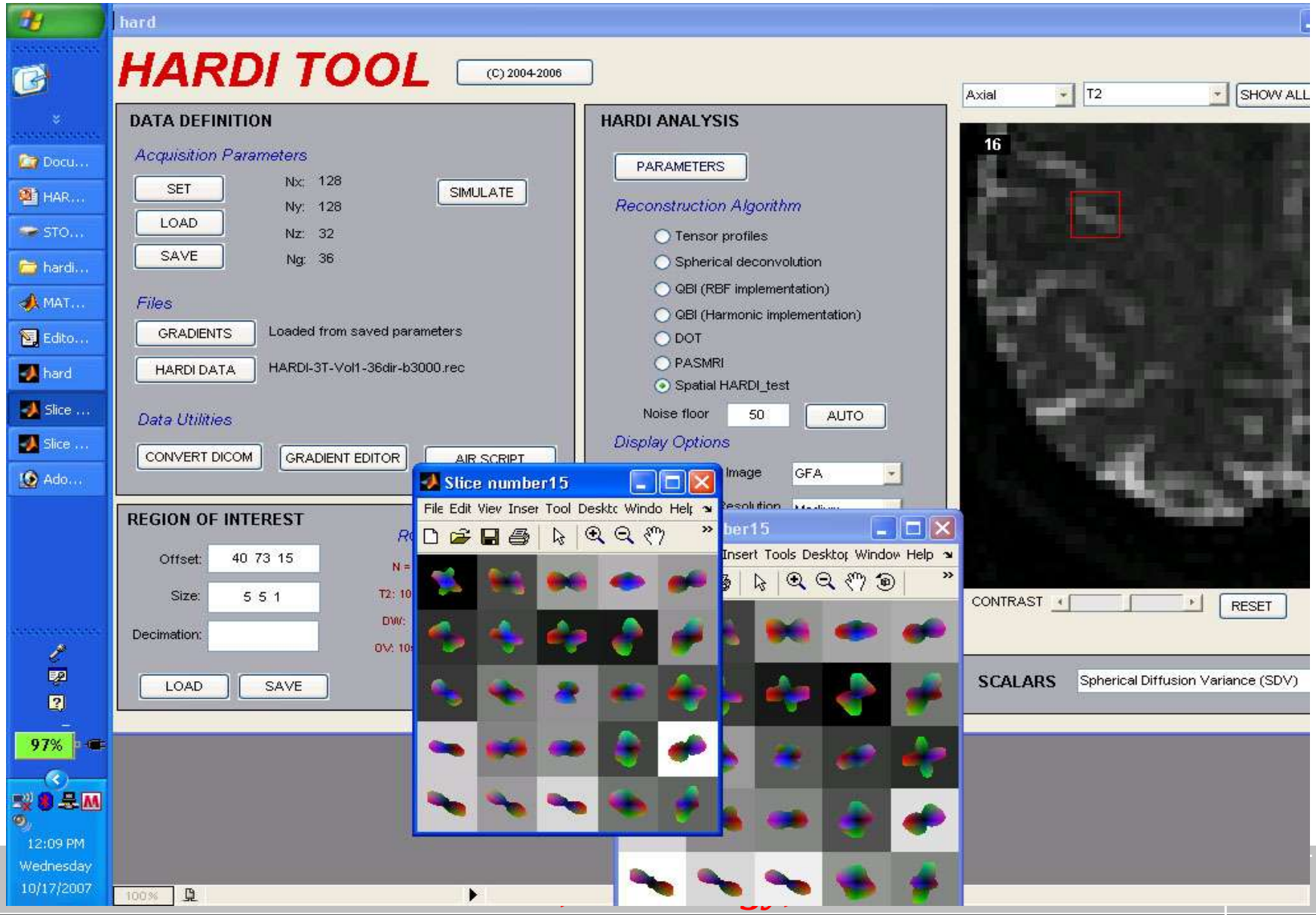
Berman JI, Chung S, Mukherjee P, Hess CP, Han ET, Henry RG. Neuroimage (2007)

Adding Spatial Constraints



- Neighbours are "like" each other, likely to have similar ODFs
- But need to allow for discontinuous boundaries

In vivo results



In vivo results

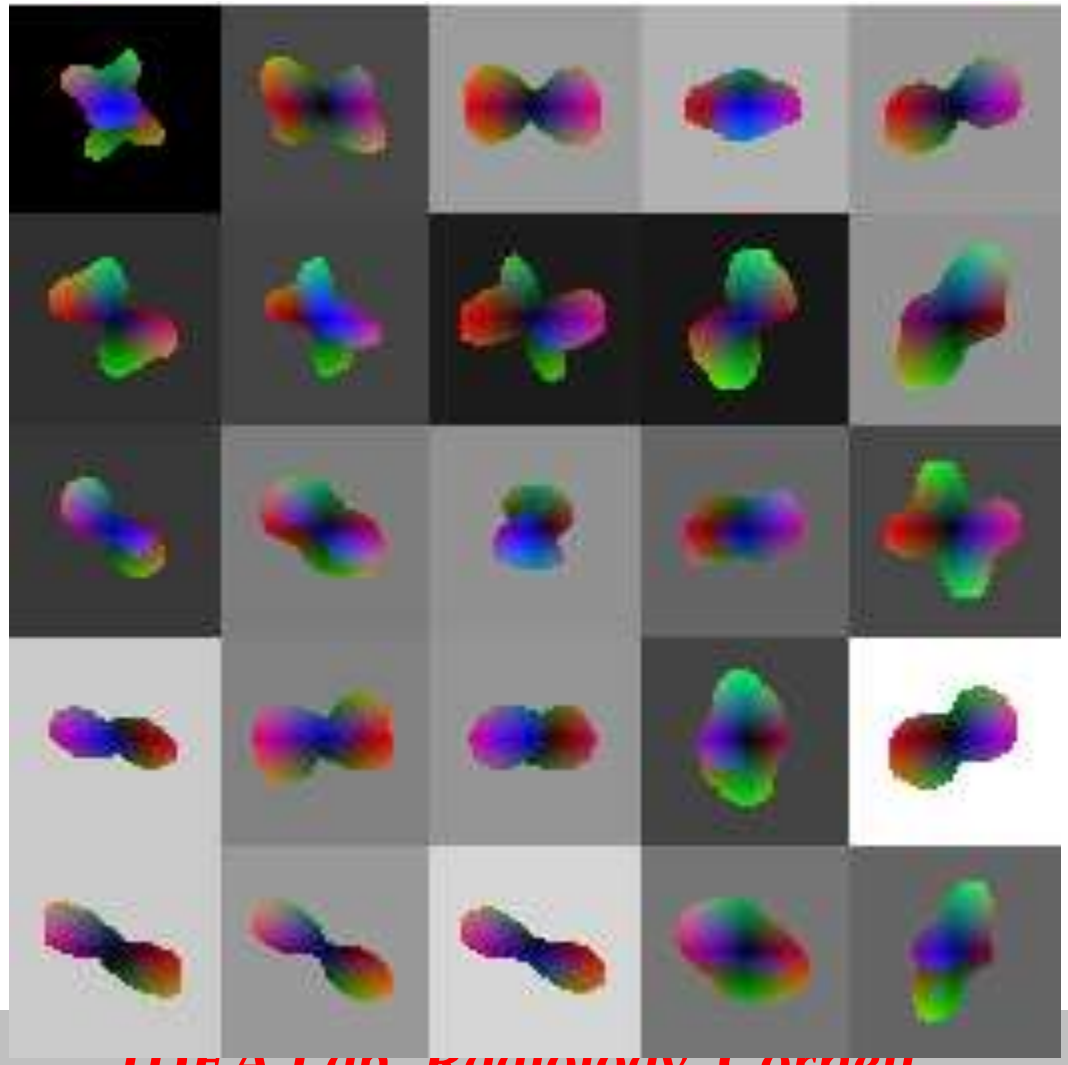
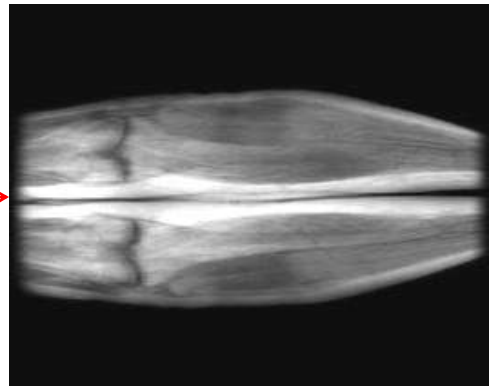


Image Reconstruction from Raw MRI data "Accelerated Imaging"

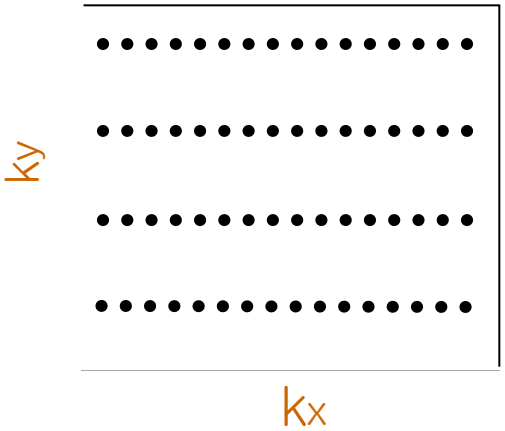
.... 0 1 1 0 1 0 1 0 1....



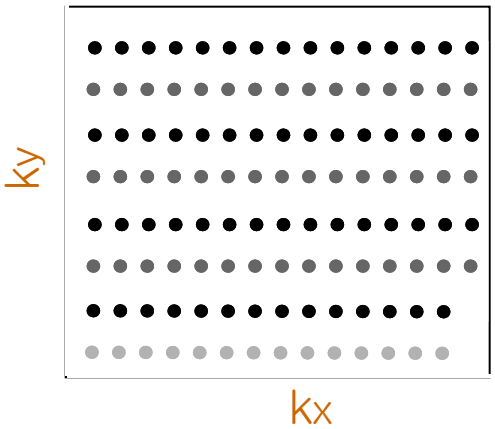
- Faster brain scans (5x speedup)
- Input: Undersampled Fourier-space raw data from scanner
- Output: Reconstructed images

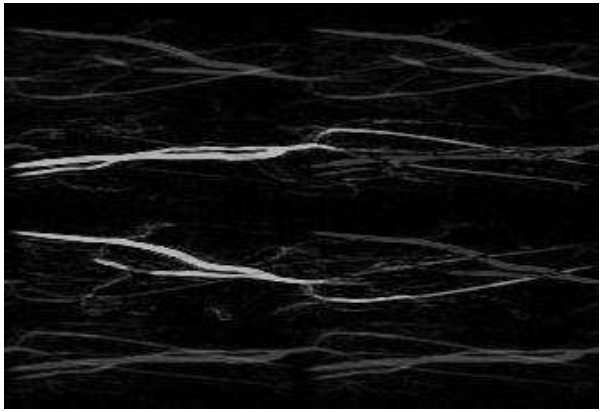
Accelerated Imaging

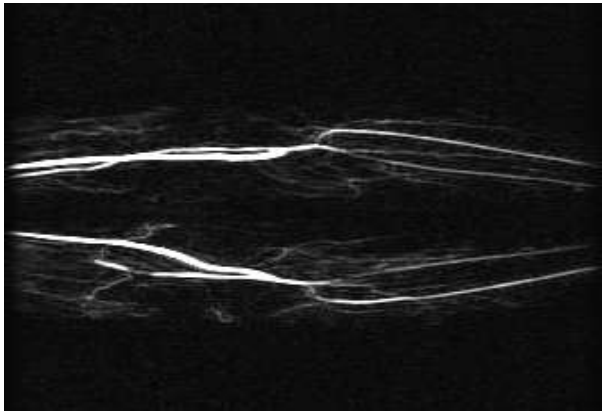
Under-sampled k-space



Reconstructed k-space

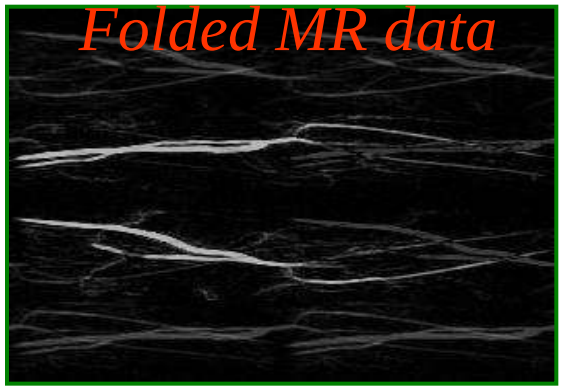


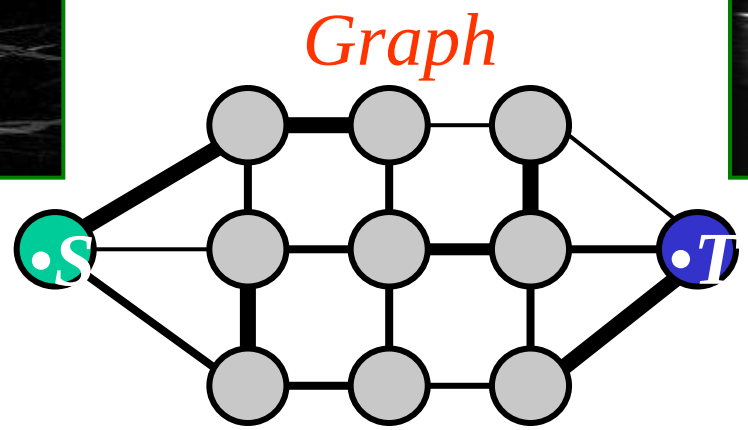


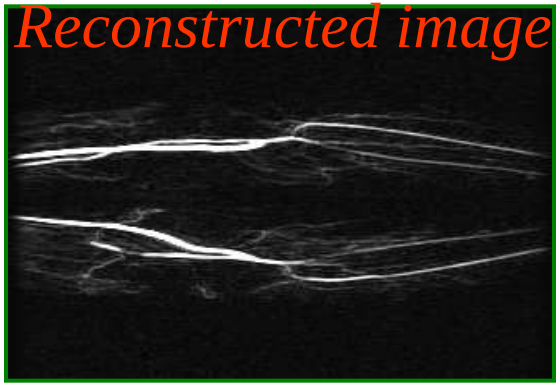


MRI Reconstruction Using Graph Cuts

- *A new graph-based algorithm **
- *Inspired by advanced robotic vision, computer science*







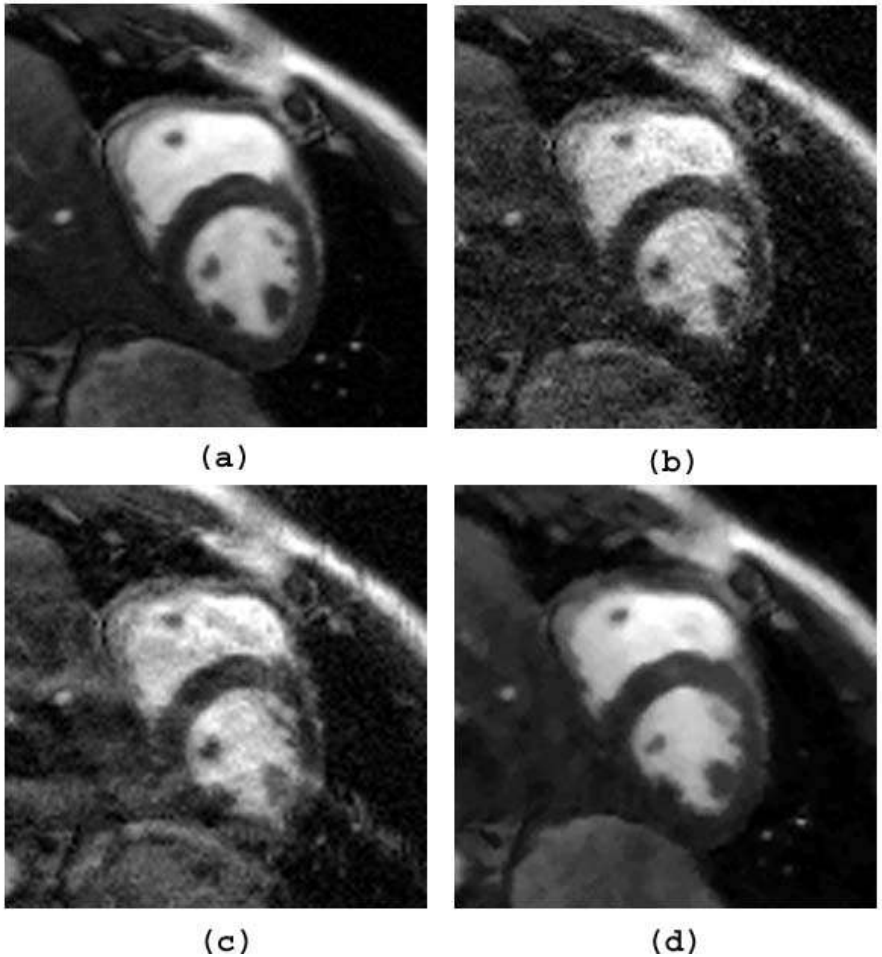
- *Operations on this graph produce reconstructed image!*

- *Raj et al, Magnetic Resonance in Medicine, Jan 2007,*
- *Raj et al, Computer Vision and Pattern Recognition, 2006*
- *Singh et al., MRM (to appear)*

Jump Move Results: Cardiac Imaging, R=4

•*reconstruction for cine SSFP at R = 4*

Reference:
Sum of squares



Regularized SENSE
(μ = 0.1)

Regularized SENSE
(μ = 0.5)

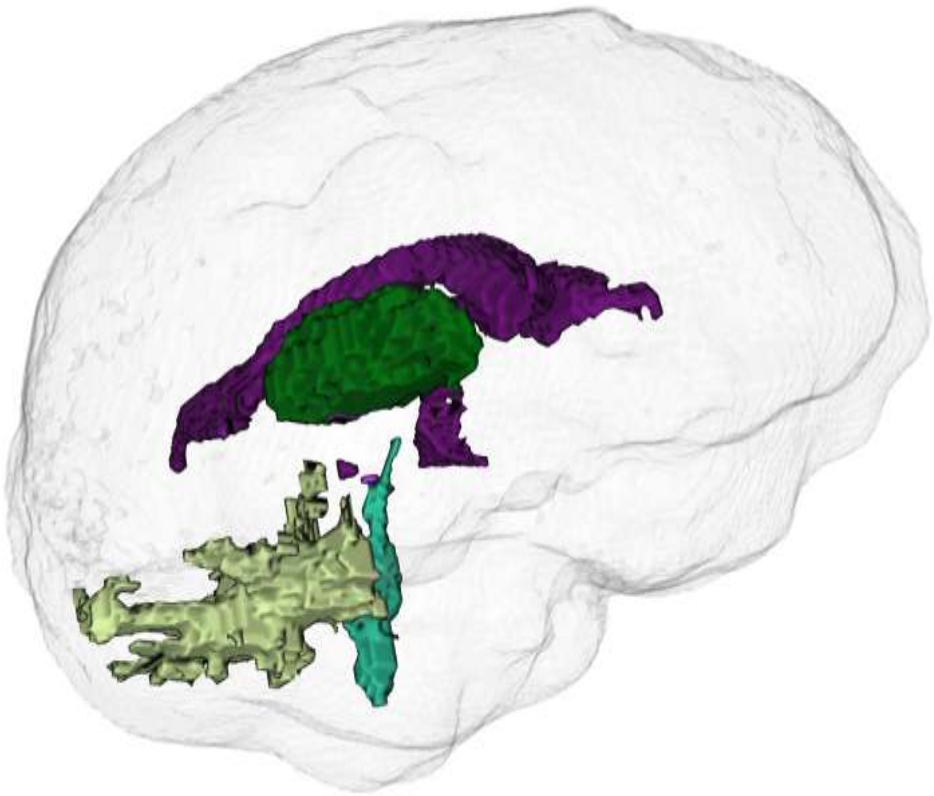
Fast EPIGRAM

Part III : Classification Examples

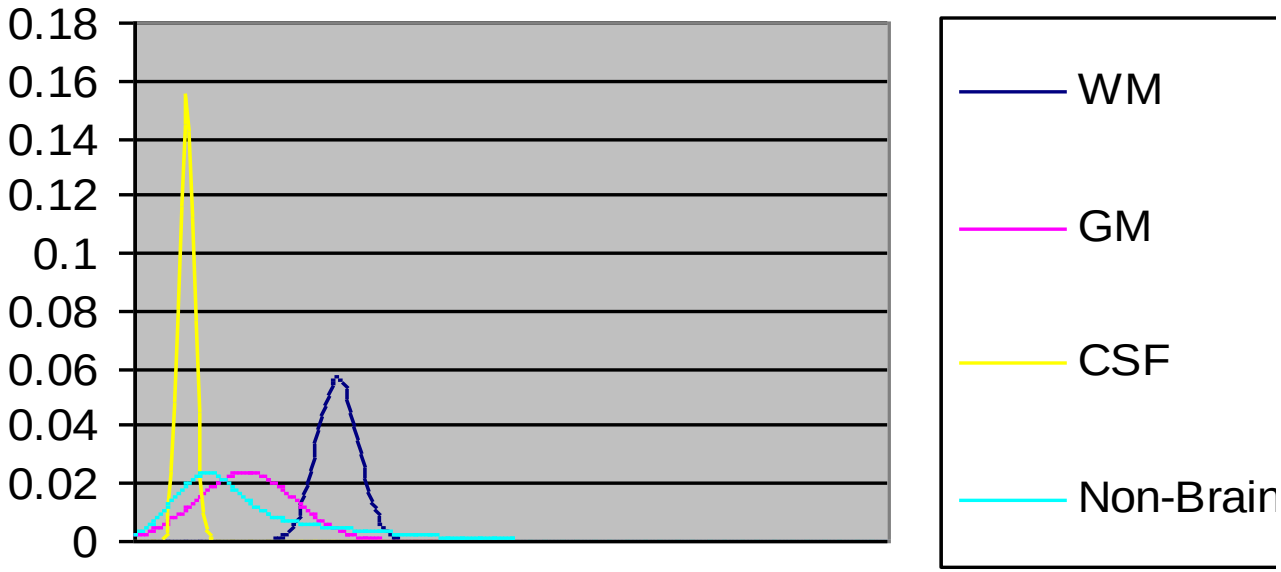
- Voxel labeling problems
- Organ labeling problems
- Patient classification problems

Neurological Disease Classification using Brain Volumetrics

- Parcellate brain MRI into various known structures and find their volumes
- Can be used for distinguishing between AD, MS, Parkinsons, Epilepsy, etc

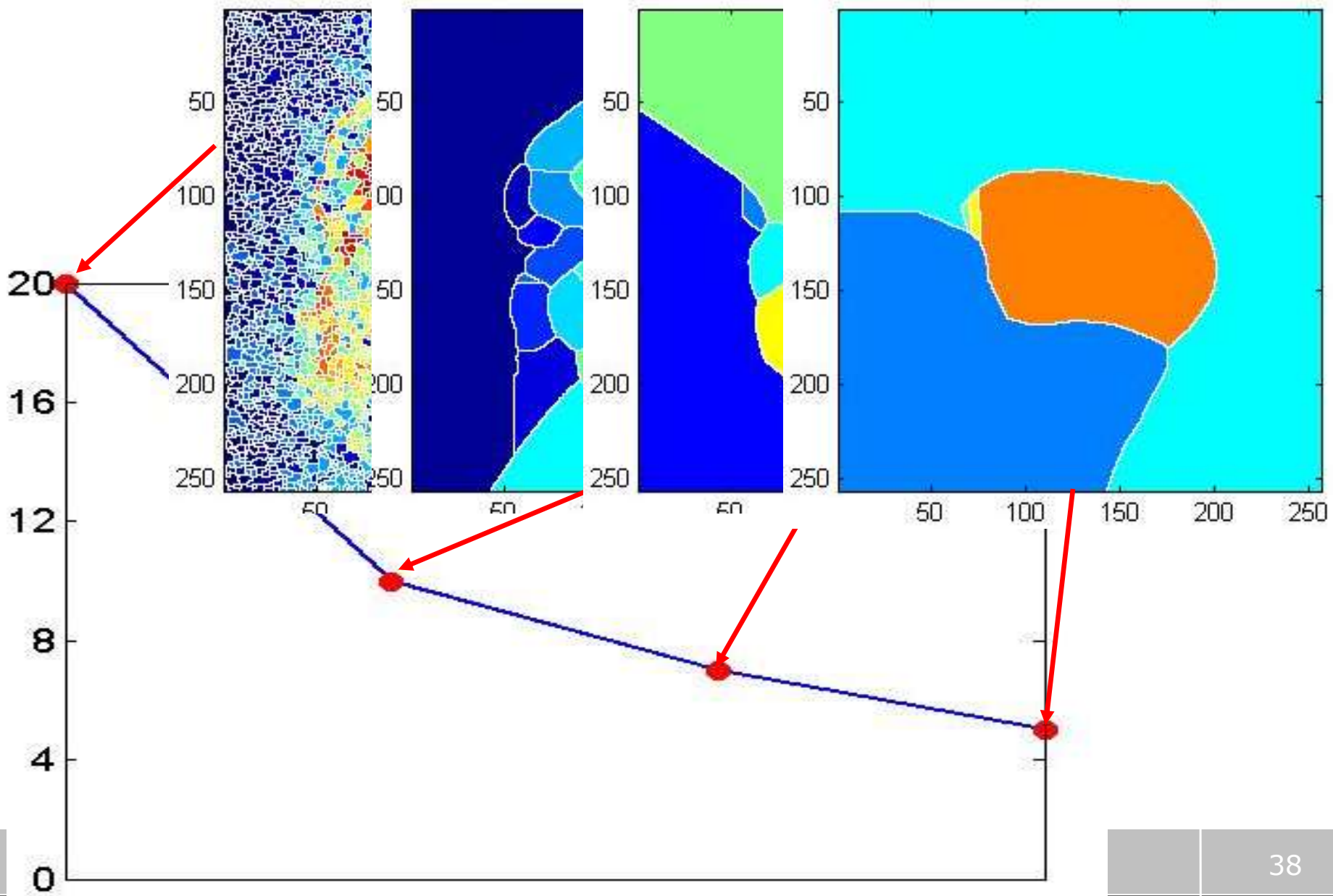


Voxel level classification: Image segmentation via Clustering

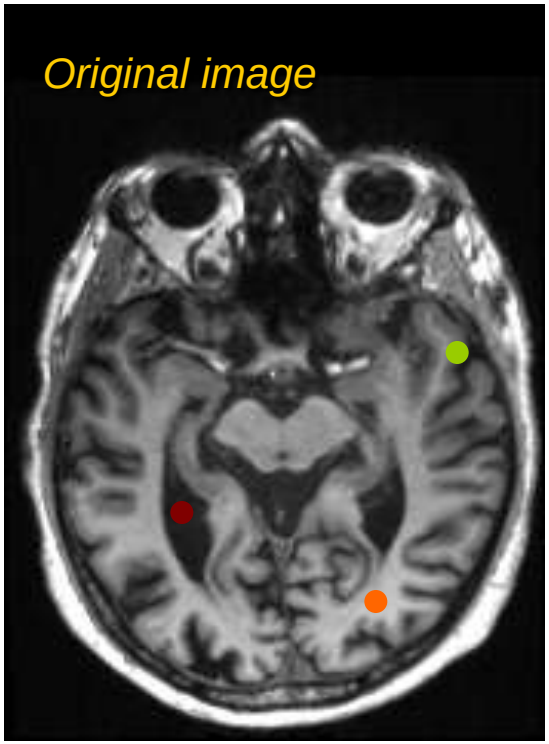


- Clustering in intensity space = thresholding
- Clustering in hybrid intensity-spatial space
- Better clustering: make use of edge info
  - use distance transform as clustering variable
- Even better: use spatial coherence

Prior Model – Driven segmentation



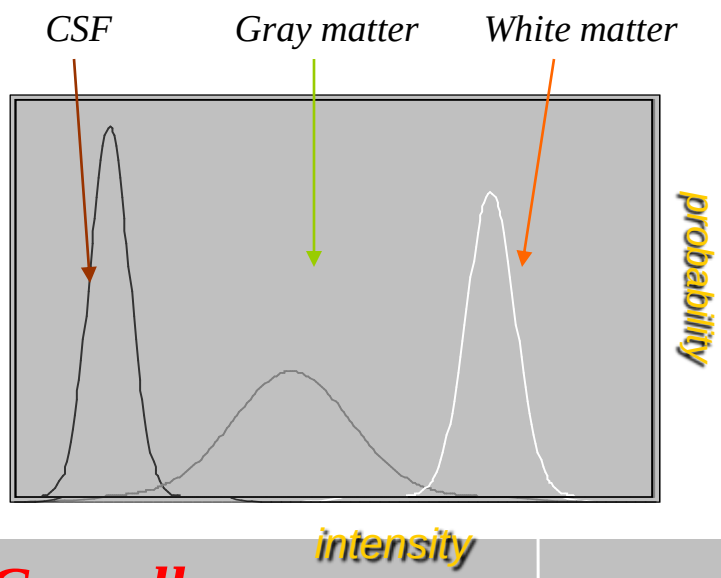
MR Segmentation Using Graph Cuts



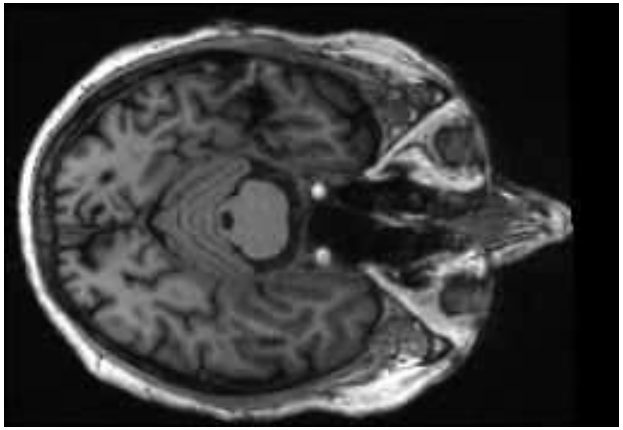
Geo Cuts

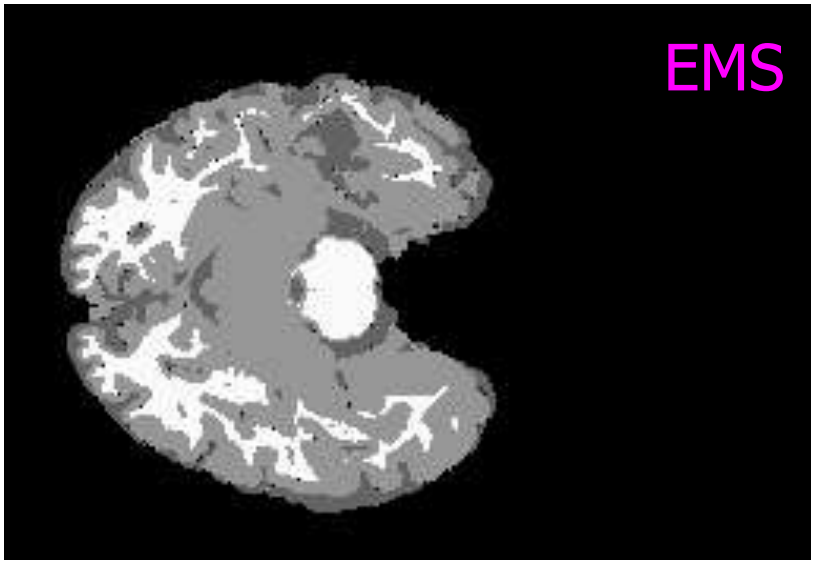
Automatically set seeds

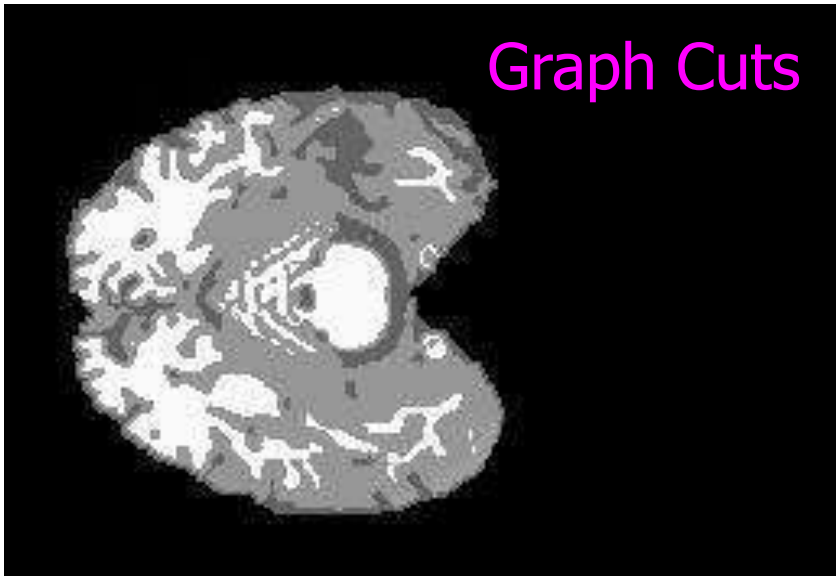
Parameter estimation



Preliminary results



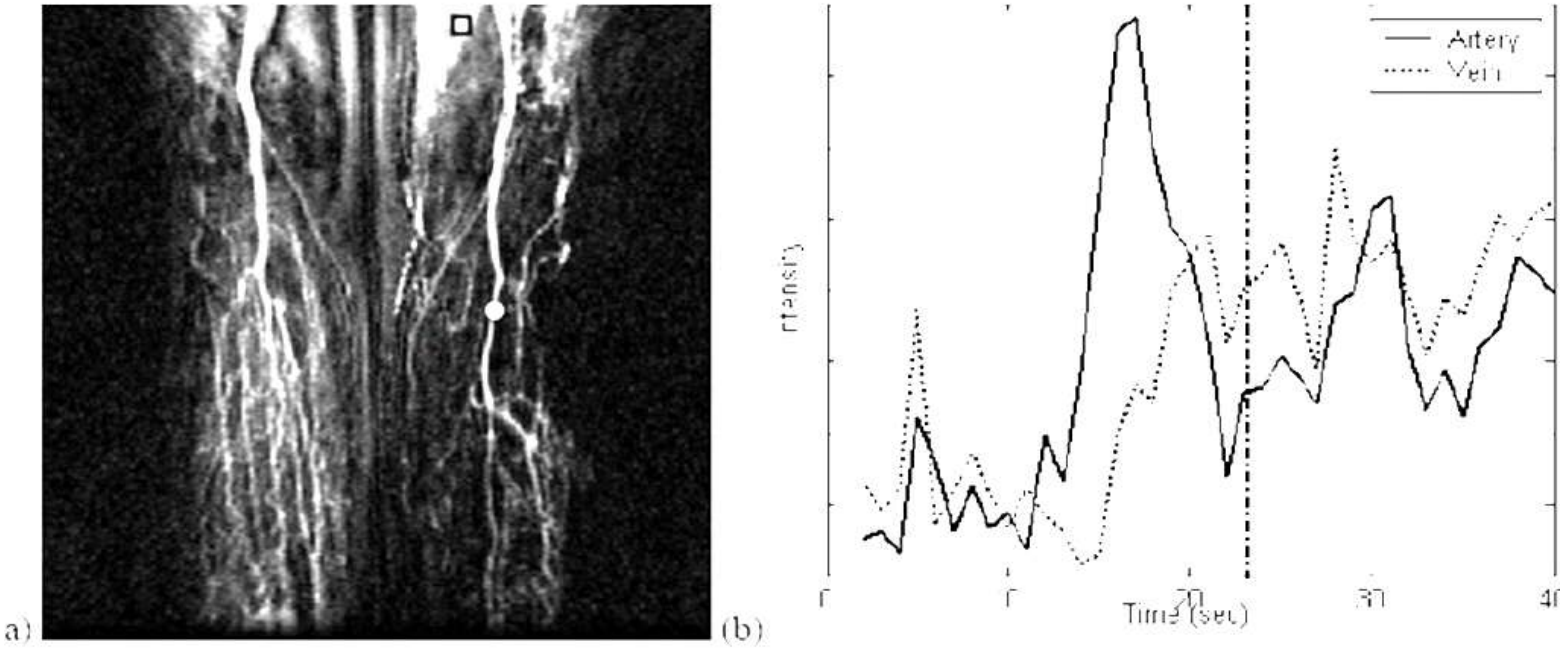




Non-intensity voxel labeling

- Can segment according to other classifications
  - activation using hemodynamic response (fMRI)
  - MR spectra
  - time profile of MR angiography data
- need to generalise the clustering approach to multilpe dimensions
- “feature space”

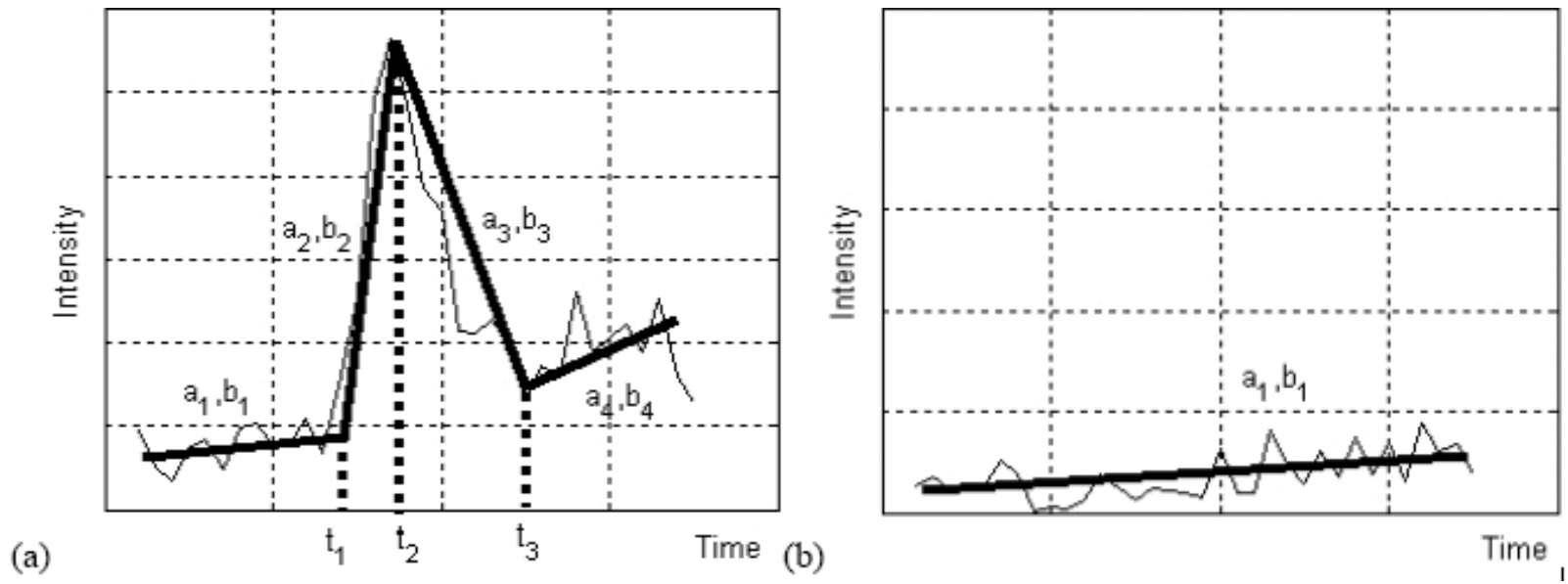
Example: MRA segmentation



- artery/vein may have similar intensity at given time point
- but different time profiles
- wish to segment according to time profile, not single intensity

Example: MRA segmentation

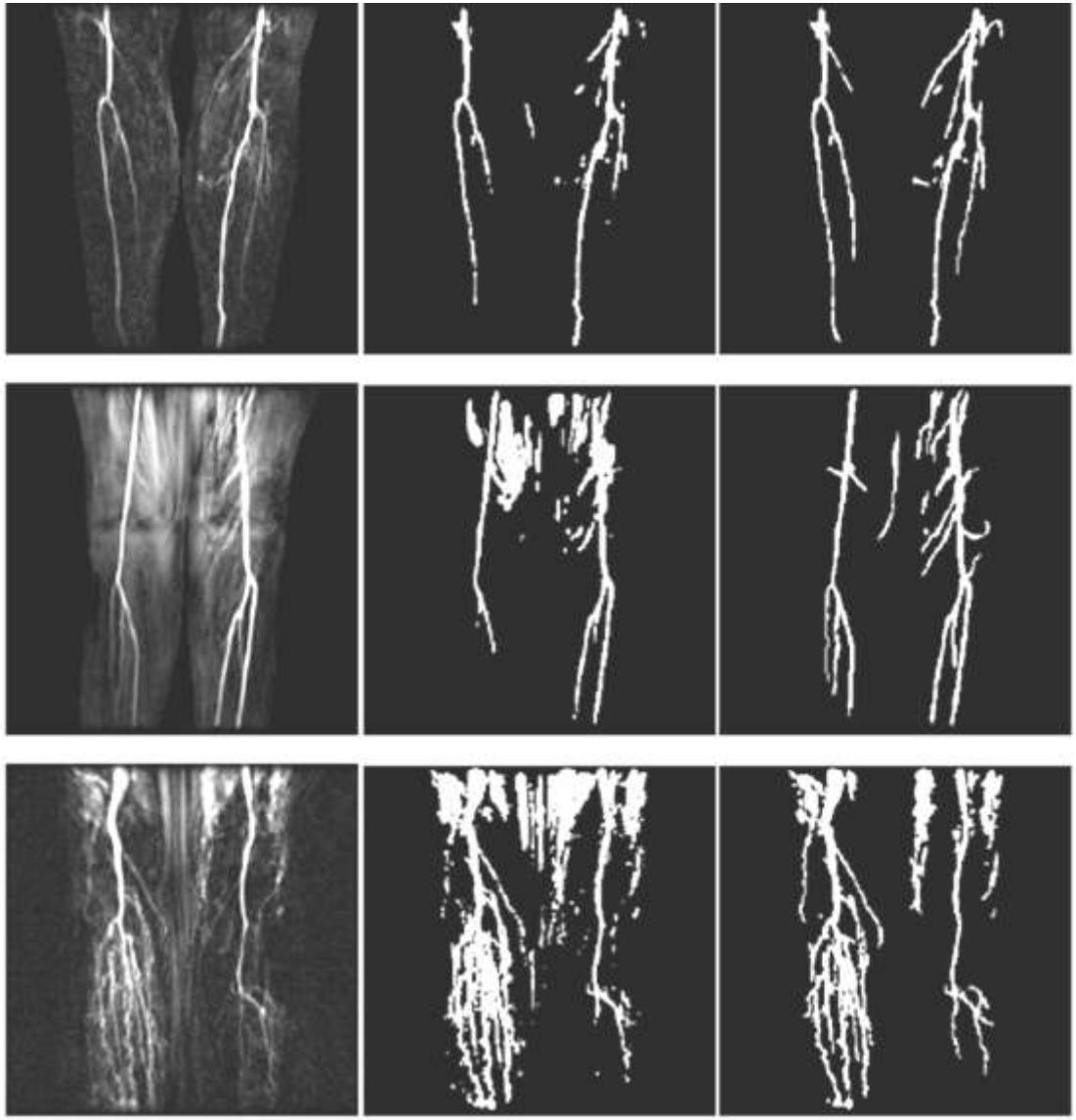
- First: need a time model of all segments!



- Next: fit observed data to these models and see which voxel belongs to which model
- (use an energy minimization framework for this)

energy = data cost + prior cost

Results



MR mammo graphy

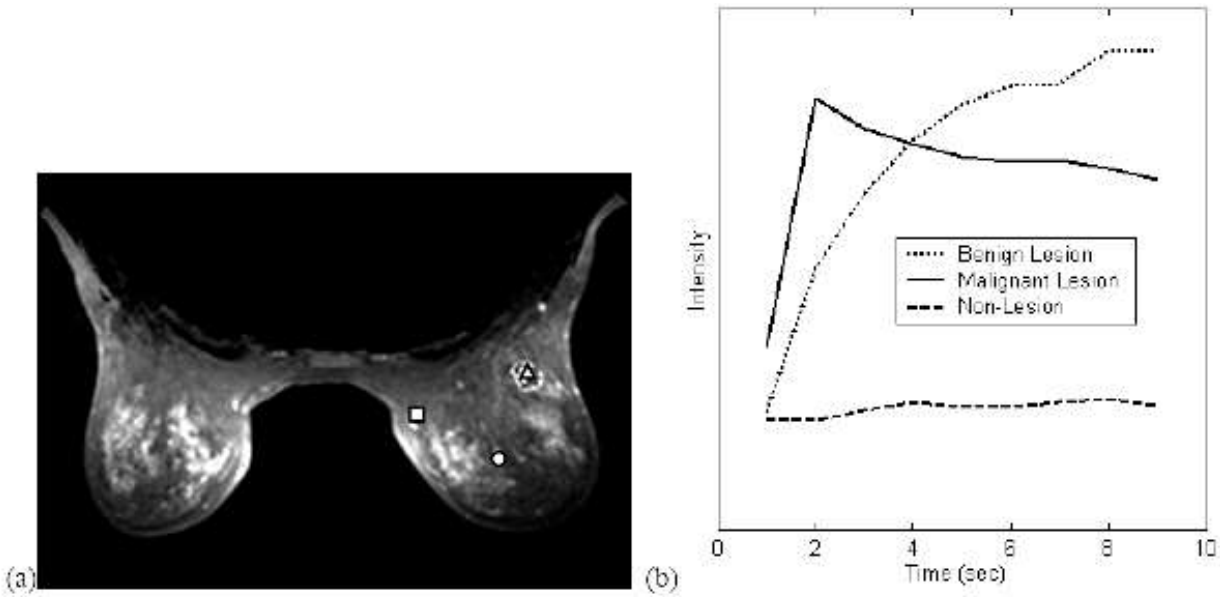


Fig. 3. (a) A snapshot of a mammography image sequence (b) Temporal profile of the selected pixels.

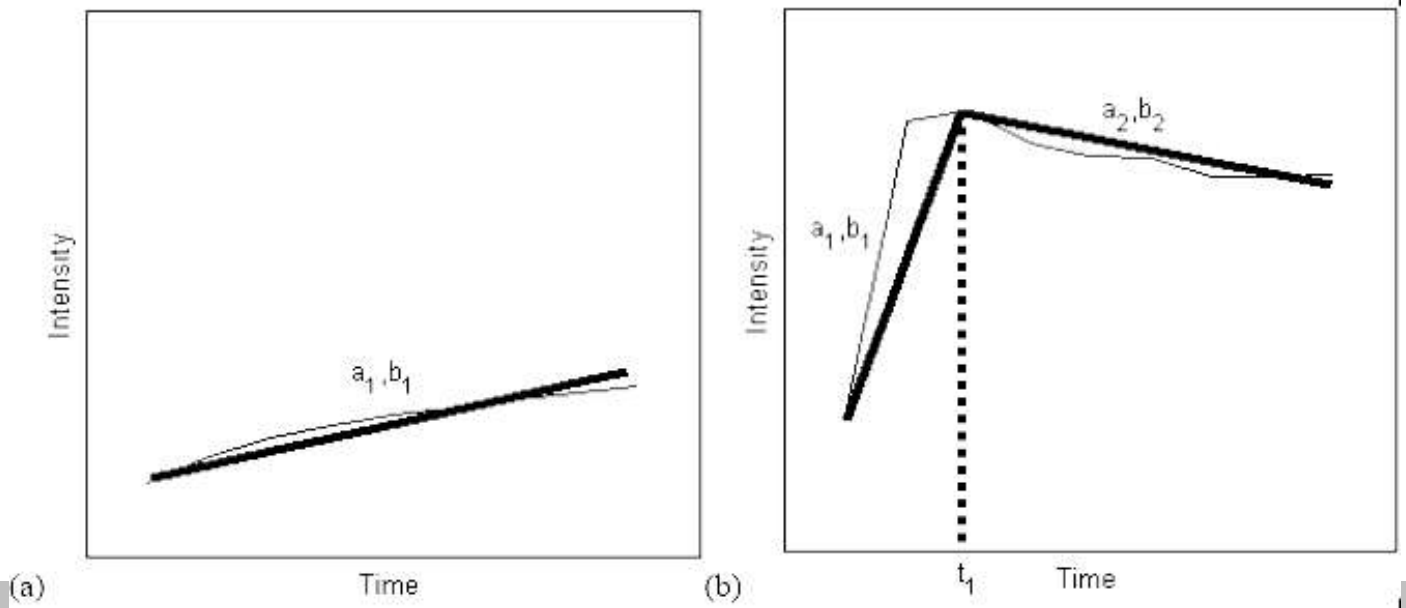
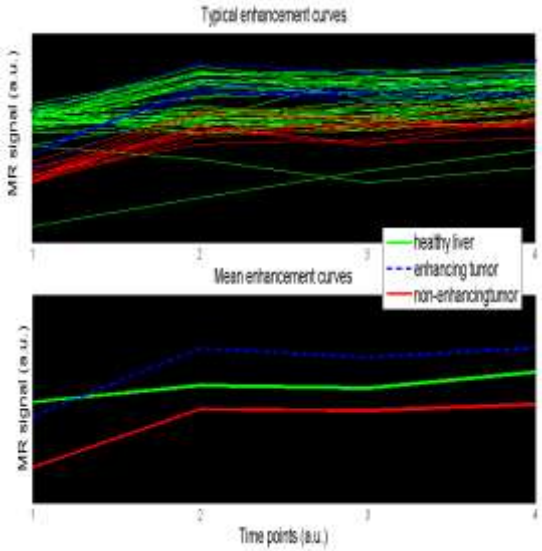


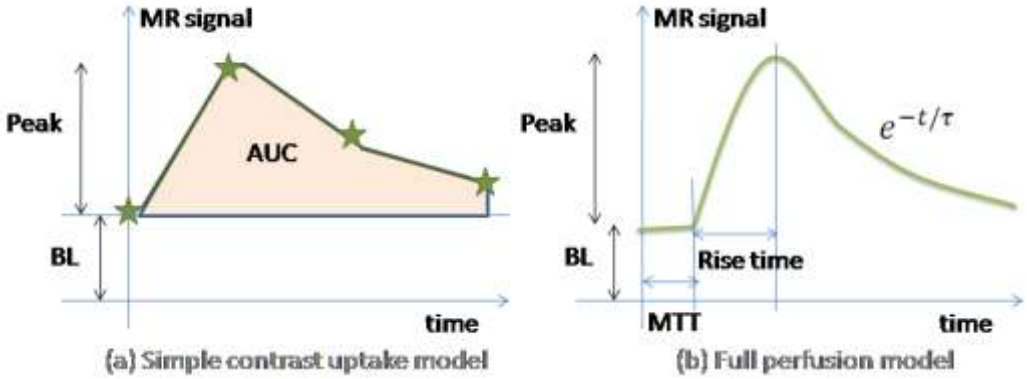
Fig. 4. Parameters for MR angiography image series (a) Lesion (b) Non-Lesion.

Liver tumour quantification from Dynamic Contrast Enhanced MRI

- Data: Tumor model Rabbit DCE-MR data
- Paramegnetic contrast agent , pathology gold standard
- Extract temporal features from DCE-MRI
- Use these features for accurate detection and quantification of tumour

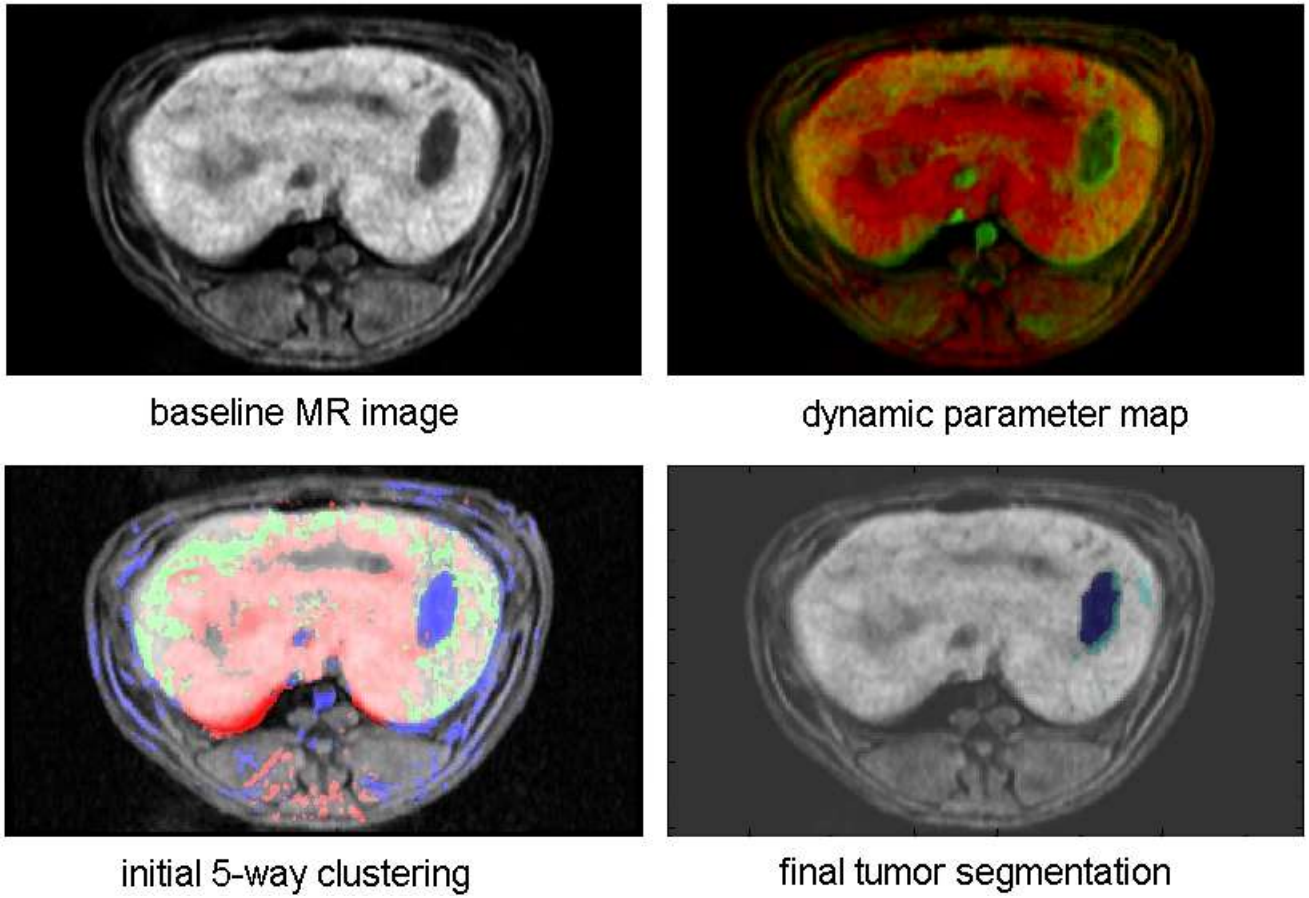


Typical plot of time-resolved MR signal of various tissue classes



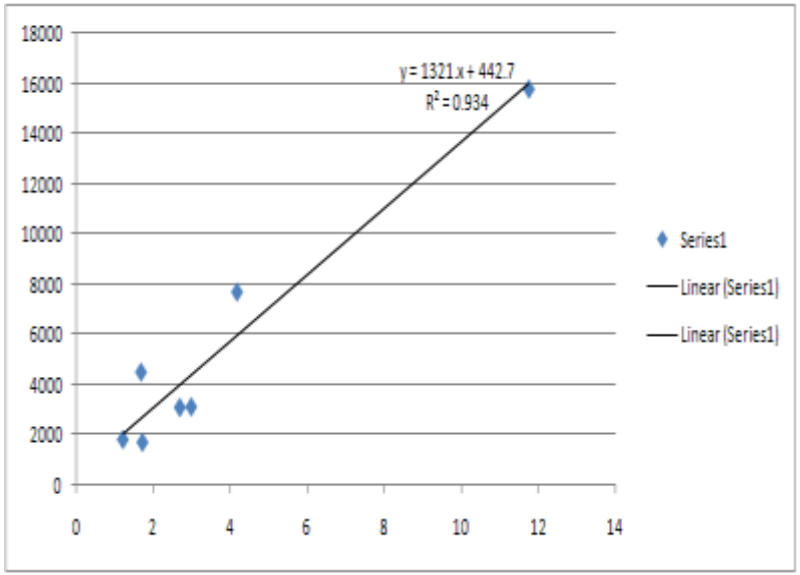
Temporal models used to extract features

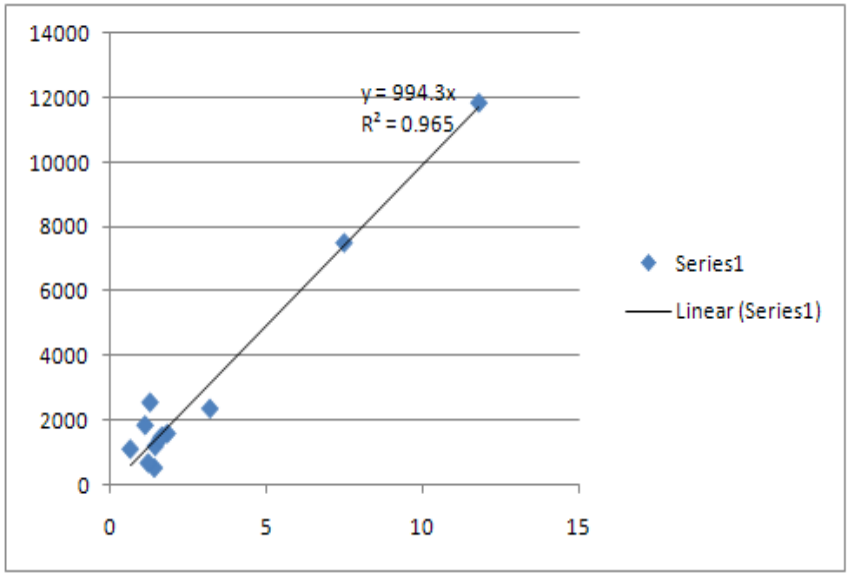
Liver tumour quantification from DCE-MRI



Preliminary Results

- Correlation plots of our volumes vs manual voluming (GE Advantage Workstation)





•*Total tumour volume*
•*(necrotic + enhancing)*

•*Necrotic tumour volume*

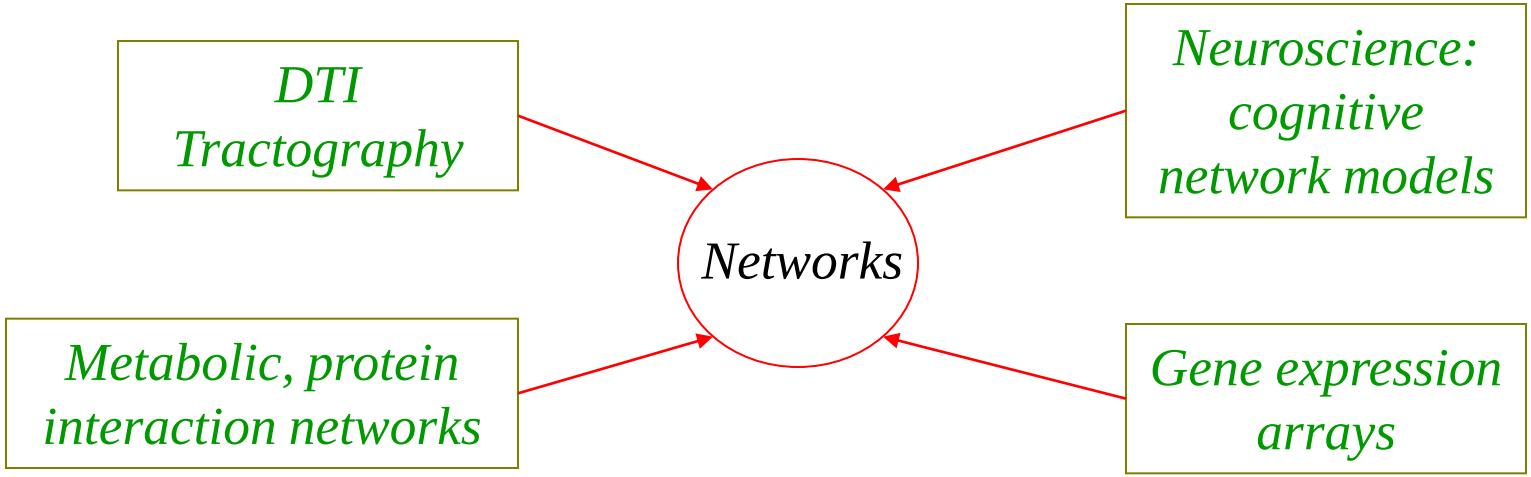
Graph-Theoretic Methods for Network-Level Analysis of Brain Imaging Data

With Thanks to:

Susanne Mueller, Karl Young (CIND/UCSF)

Biological networks

- Networks are EVERYWHERE
- Network analysis is going to be the next big thing in biology



"The connection matrix of the human brain (the human "connectome") represents an indispensable foundation for basic and applied neurobiological research."
- From Sporns, Tononi and Kotter, "The Human Connectome: A Structural Description of the Human Brain", PLoS Computational Bioogy 2005

Structural Brain Network from Fiber Tracing – Macaque Brain (Cocomac Project)

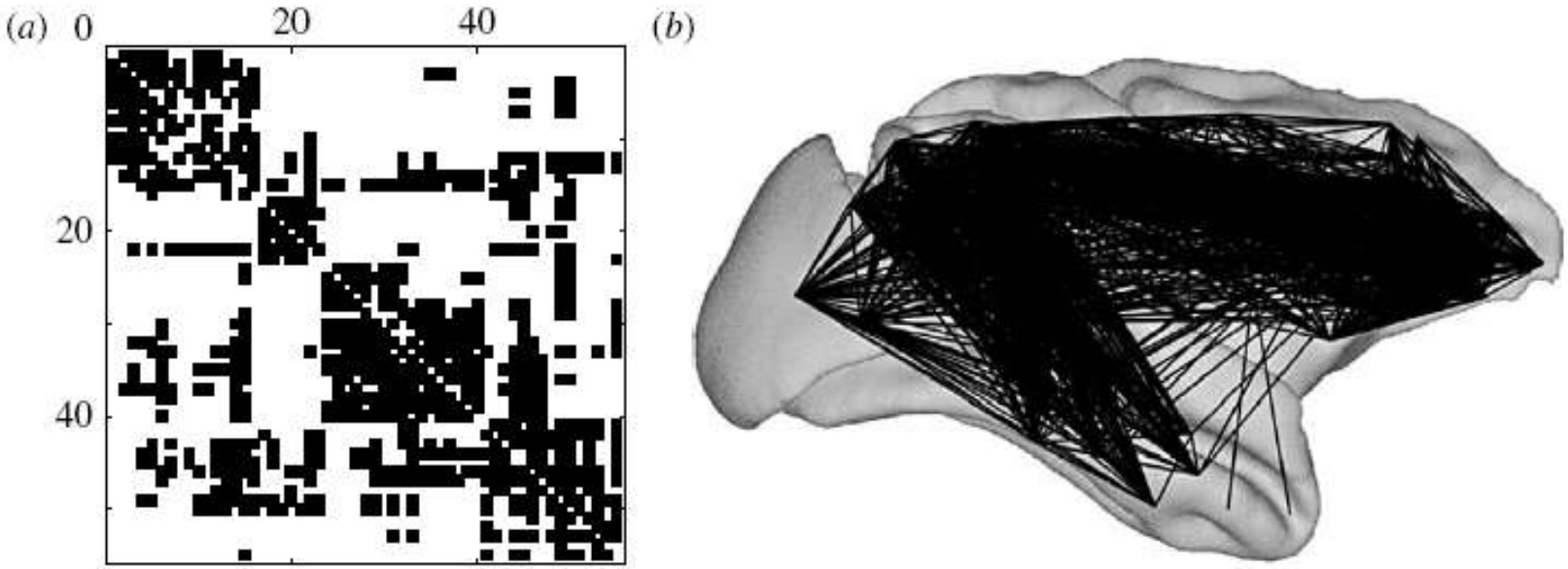
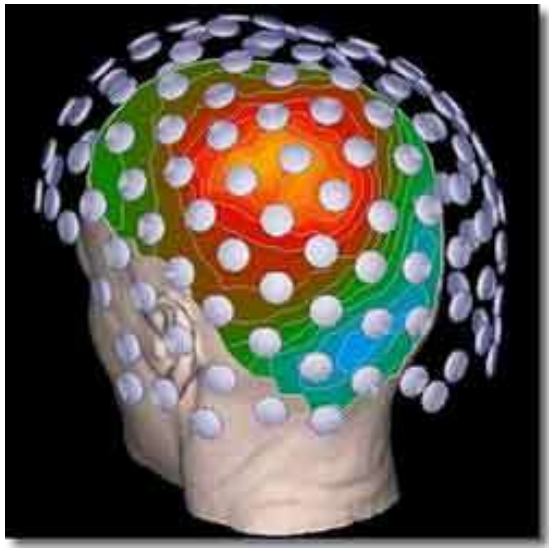
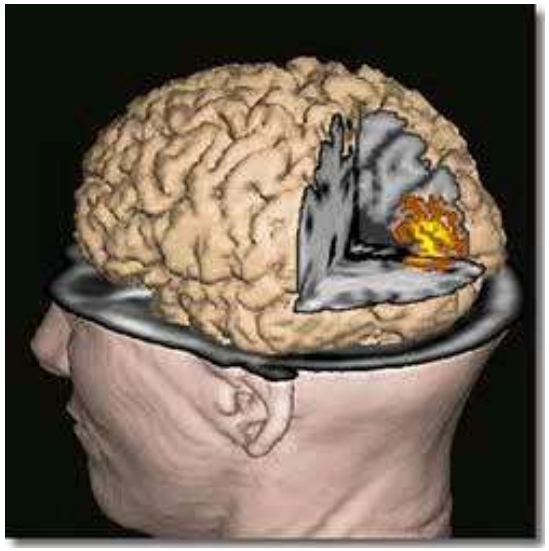


Figure 1. (*a*) Adjacency matrix of the cat connectivity network (55 nodes; 891 directed edges). Dots represent '1' and white spaces the '0' entries of the adjacency matrix. (*b*) Macaque cortex (95 nodes; 2402 directed edges).

MARCUS KAISER. Brain architecture: a design for natural computation. Phil. Trans. R. Soc. A, 2007.

Networks from MagnetoEncephaloGraphy





- Some recent work on this – Honey and Sporns, Fox, etc
- Time-resolved MEG signal → tomographic reconstruction → source localization → extract connectivity network
- Connectivity = correlation between MEG signals

The human brain is intrinsically organized into dynamic, anticorrelated functional networks
Michael D. Fox, Abraham Z. Snyder, Justin L. Vincent, Maurizio Corbetta, David C. Van Essen, and Marcus E. Raichle. PNAS 2005

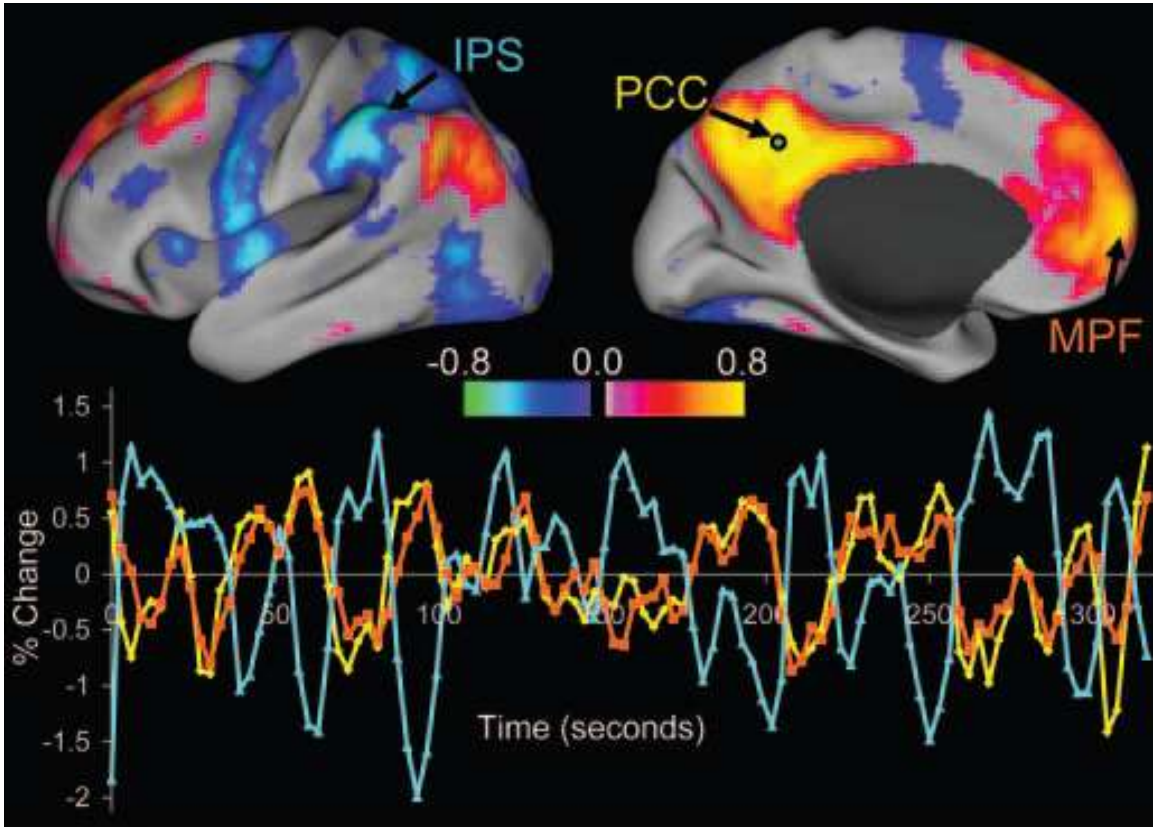
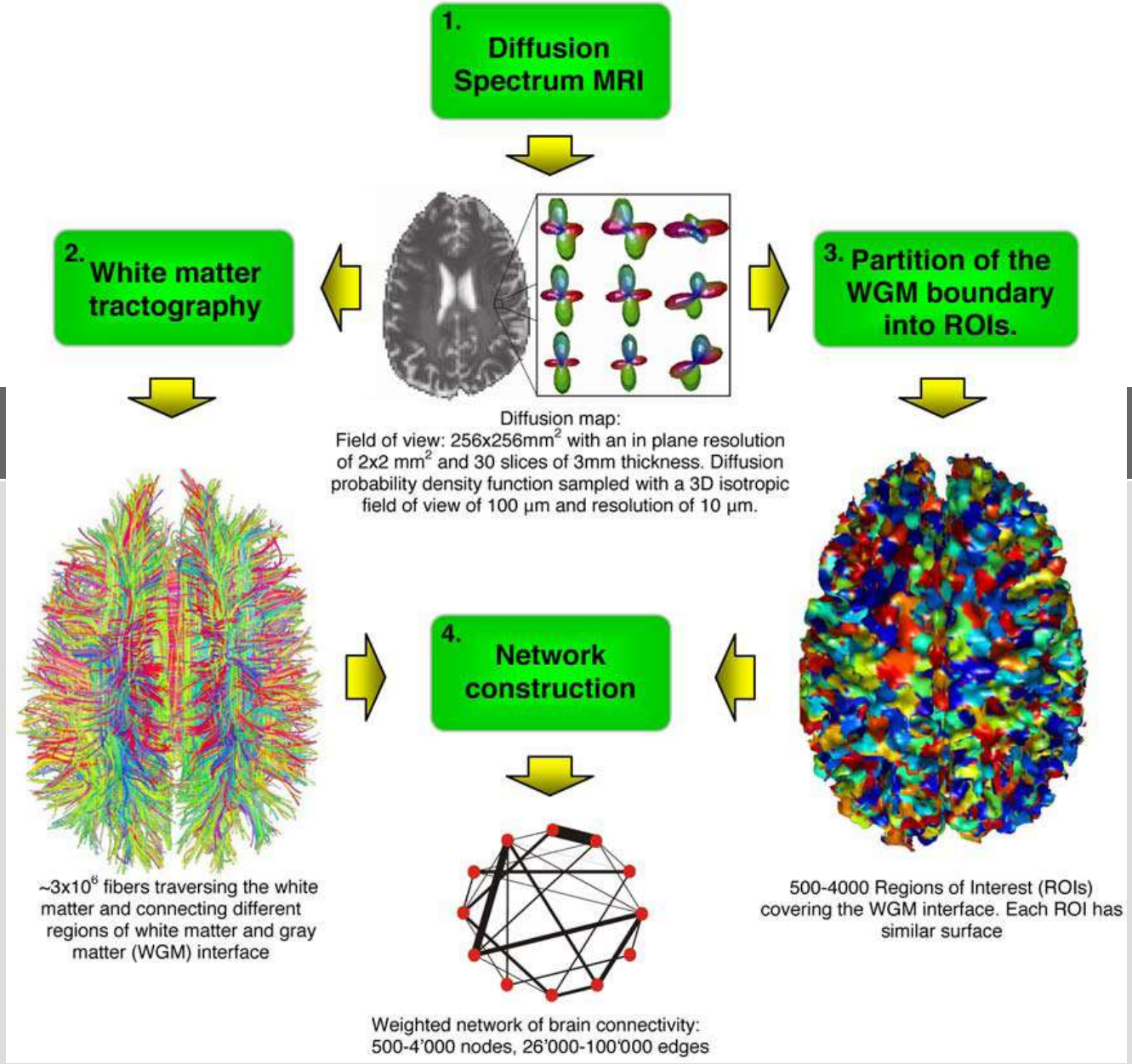


Fig. 1. Intrinsic correlations between a seed region in the PCC and all other voxels in the brain for a single subject during resting fixation. The spatial distribution of correlation coefficients shows both correlations (positive values) and anticorrelations (negative values), thresholded at *R* 0.3. The time course for a single run is shown for the seed region (PCC, yellow), a region positively correlated with this seed region in the MPF (orange), and a region negatively correlated with the seed region in the IPS (blue).

Networks from Diffusion MRI

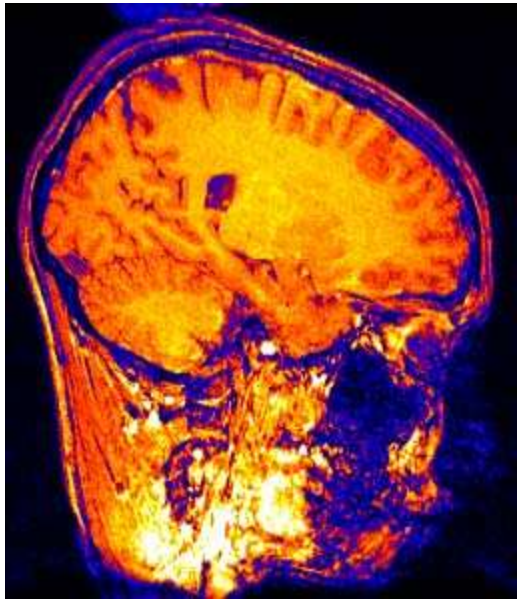
- Obtain WM tracts from DTI/HARDI/DSI using tractography
- From tracts terminating in cortical ROIs, estimate the strength of "connection" between them
  - Examples: Medina-Iterria in NeuroImage, Hagmann in PLoS One 2(7), etc
- This gives the connectivity matrix, hence the network



Mapping Human Whole-Brain Structural Networks with Diffusion MRI
Patric Hagmann, Maciej Kurant, Xavier Gigandet, Patrick Thiran, Van J. Wedeen, Reto Meuli, Jean-Philippe Thiran, PLoS ONE 2(7)

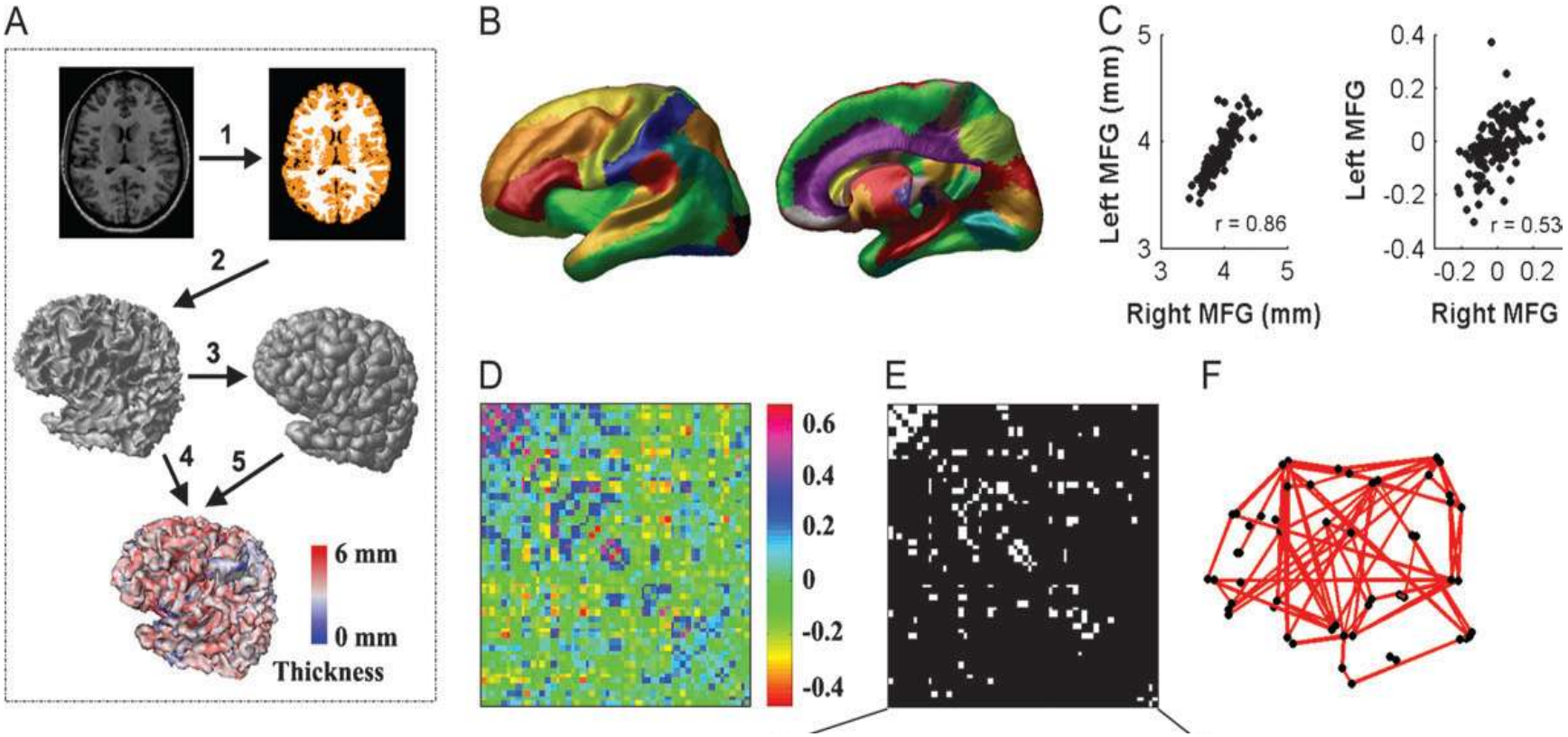
Cortical Thickness Network from Brain MRI

1. Acquire MRI of brain
2. Segment GM/WM/CSF/nonbrain
3. Parcellate GM into ROI's based on anatomy (gyri and sulci)



- Idea: cortical thickness of various ROIs are not independent but may be correlated across subjects
- Each ROI gets a node in the graph
- Define edge weight between node i and node j as the strength of correlation between ROI_i and ROI_j

Cortical Thickness Network



Yong He, Zhang J. Chen and Alan C. Evans. Small-World Anatomical Networks in the Human Brain Revealed by Cortical Thickness from MRI.
Cerebral Cortex October 2007;17:2407--2419

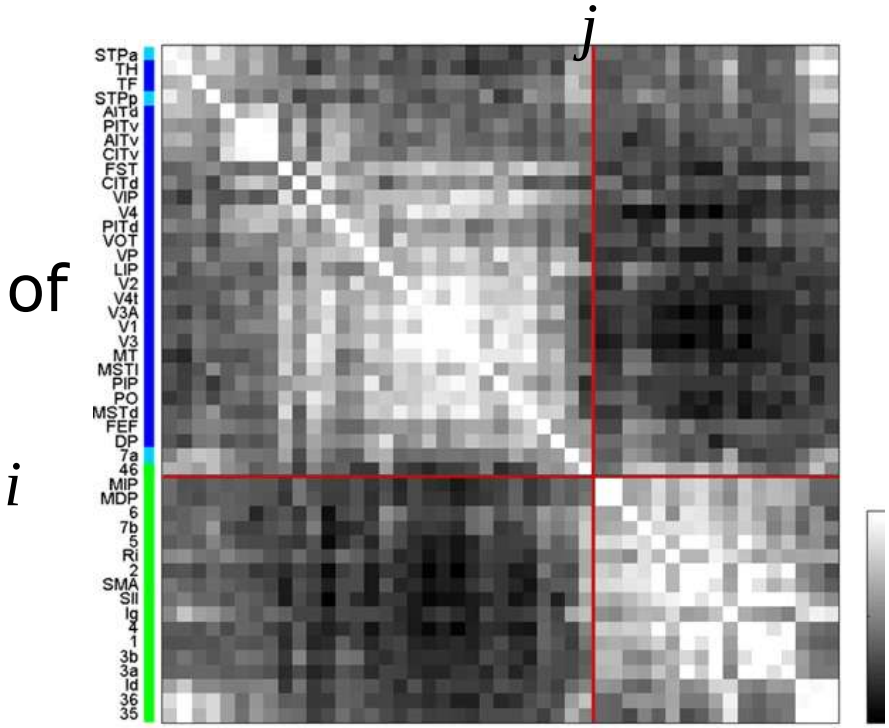
Cortical thickness networks in Epilepsy

Xi(k) = average thickness of *i*-th ROI of *k*-th subject
Si = standard deviation of *i*-th ROI, from all 31 healthy subjects
Mi = mean over all 31 healthy subjects

$$z_i(k) = (x_i(k) - m_i) / s_i$$

$$[C(k)]_{i,j} = |z_i(k) - z_j(k)|$$

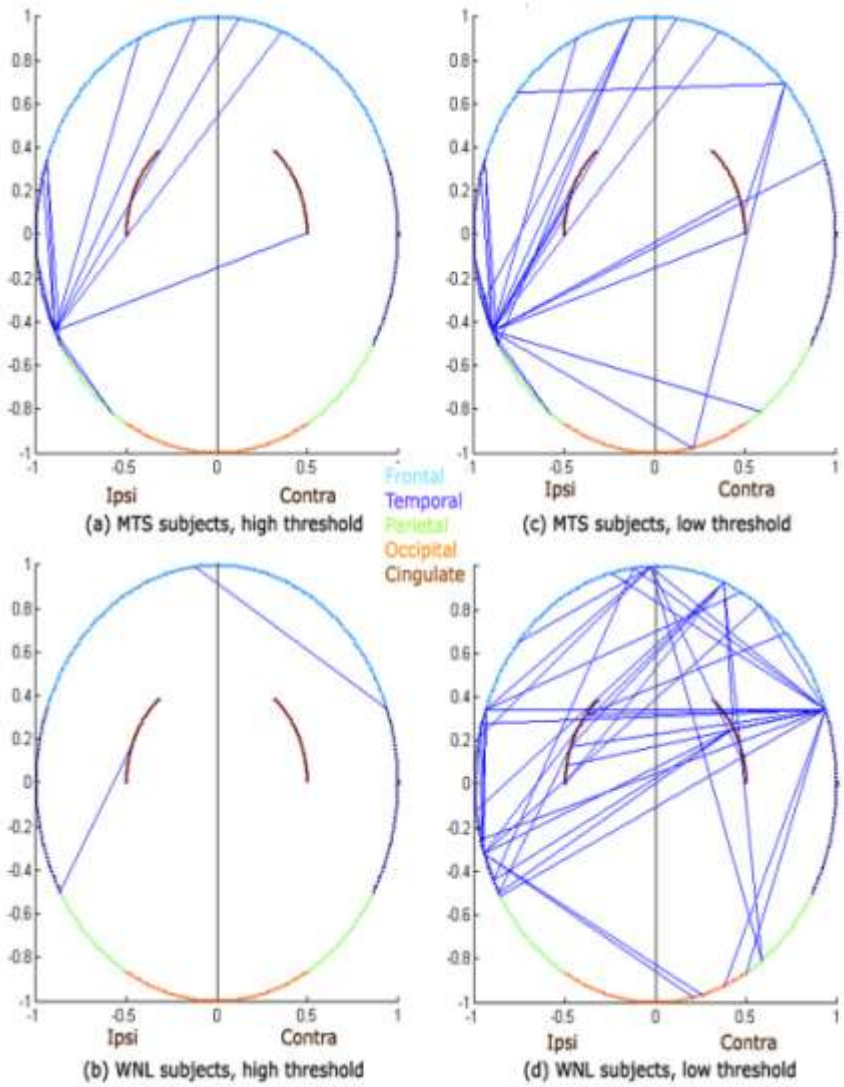
- $C(k)$ = connectivity matrix of subject k



Group Networks

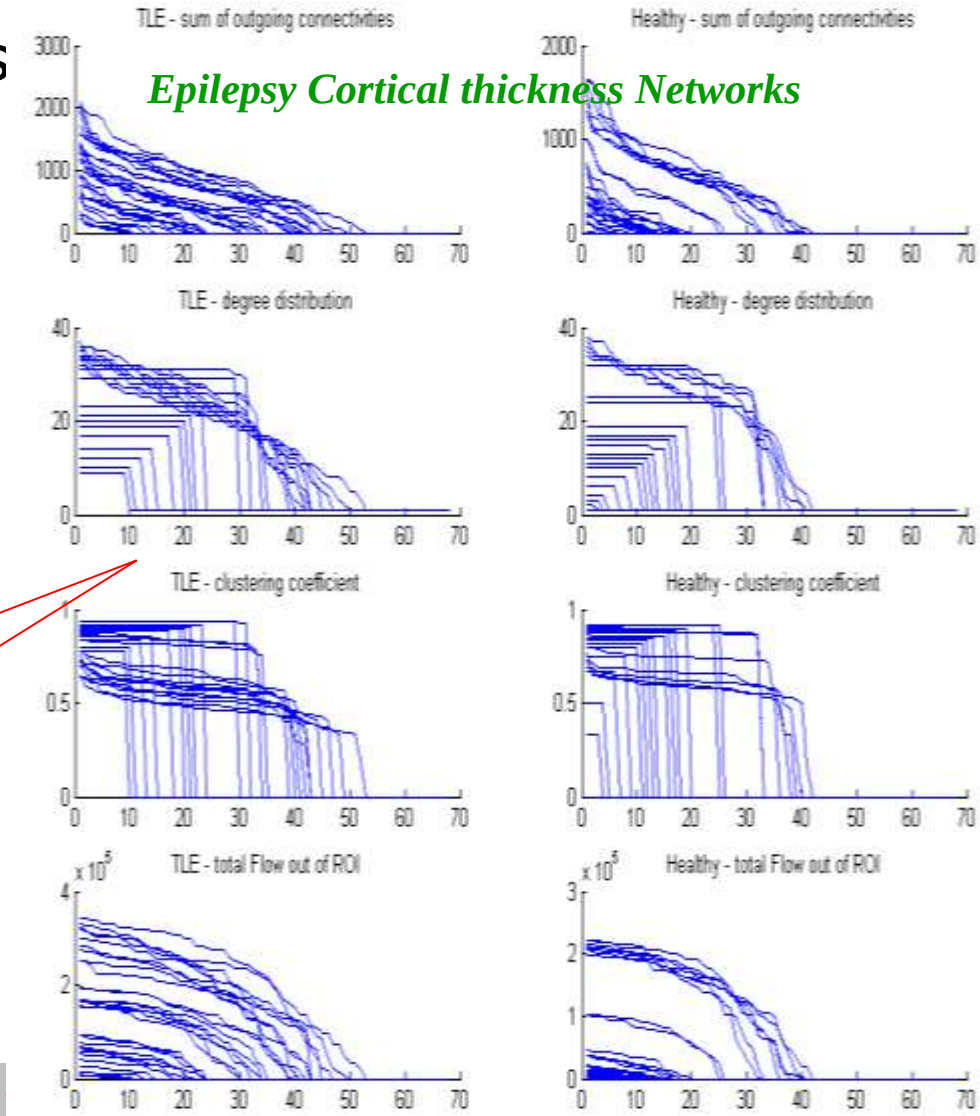
MTS

WNL



Can we use single-network statistics to differentiate population of networks?

- Compile network stats for each subject:
  - Degree distribution
  - Clustering index
  - path-length
- Perform classification using these stats as feature vector

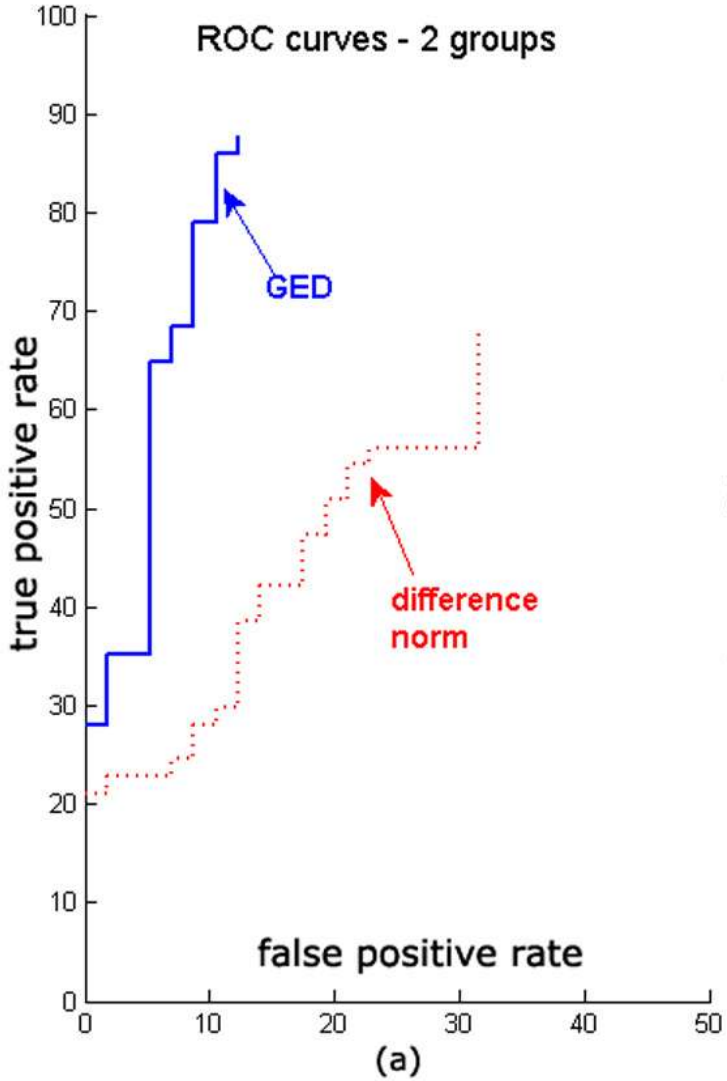


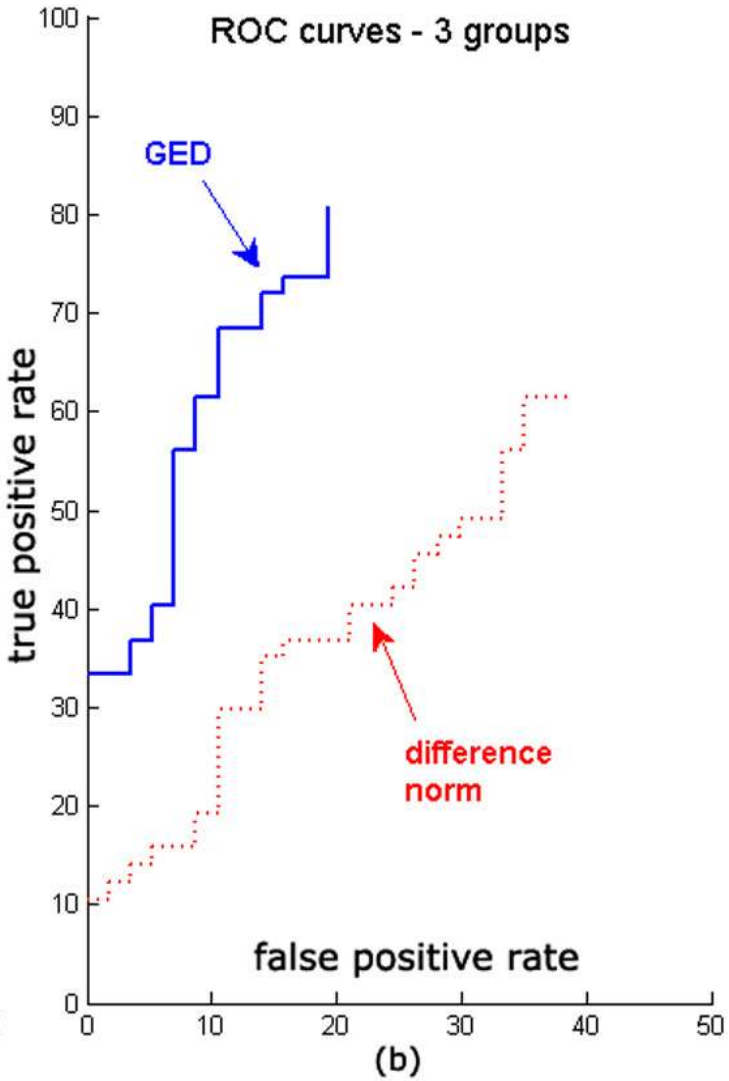
Conventional network summary variables don't work!
We need some other means of distinguishing between networks

Population of Networks – Graph Theory Approach

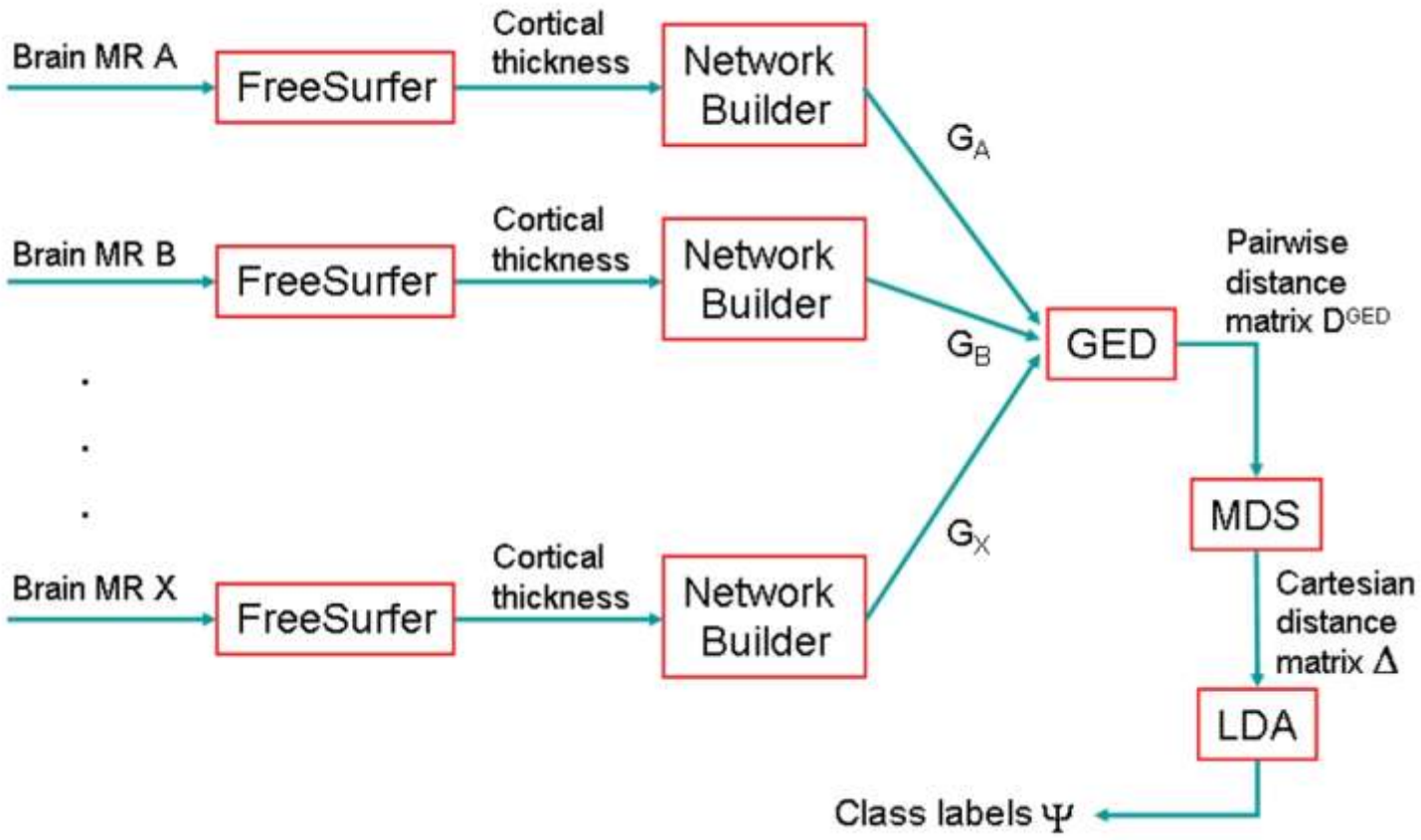
- New work: proposing a new approach for comparing networks
- Given graphs G_A and G_B, define the GRAPH EDIT DISTANCE between them as:
  - Start from G_A, and insert/delete nodes and edges in order to convert G_A into G_B
  - The cost of each insertion or deletion is predetermined
  - The smallest total cost of this procedure = GED

Epilepsy Network Classification – 2/3 Groups

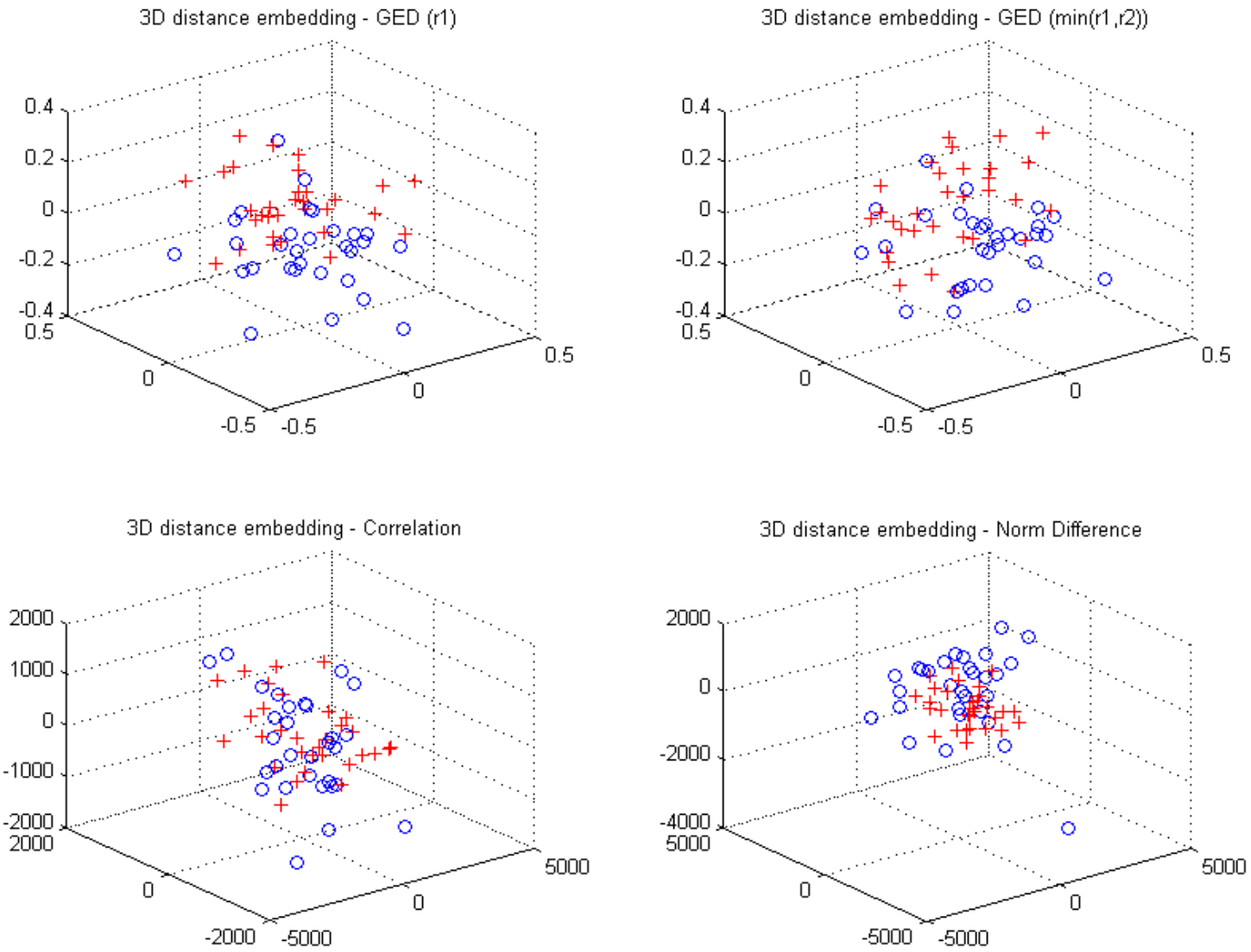




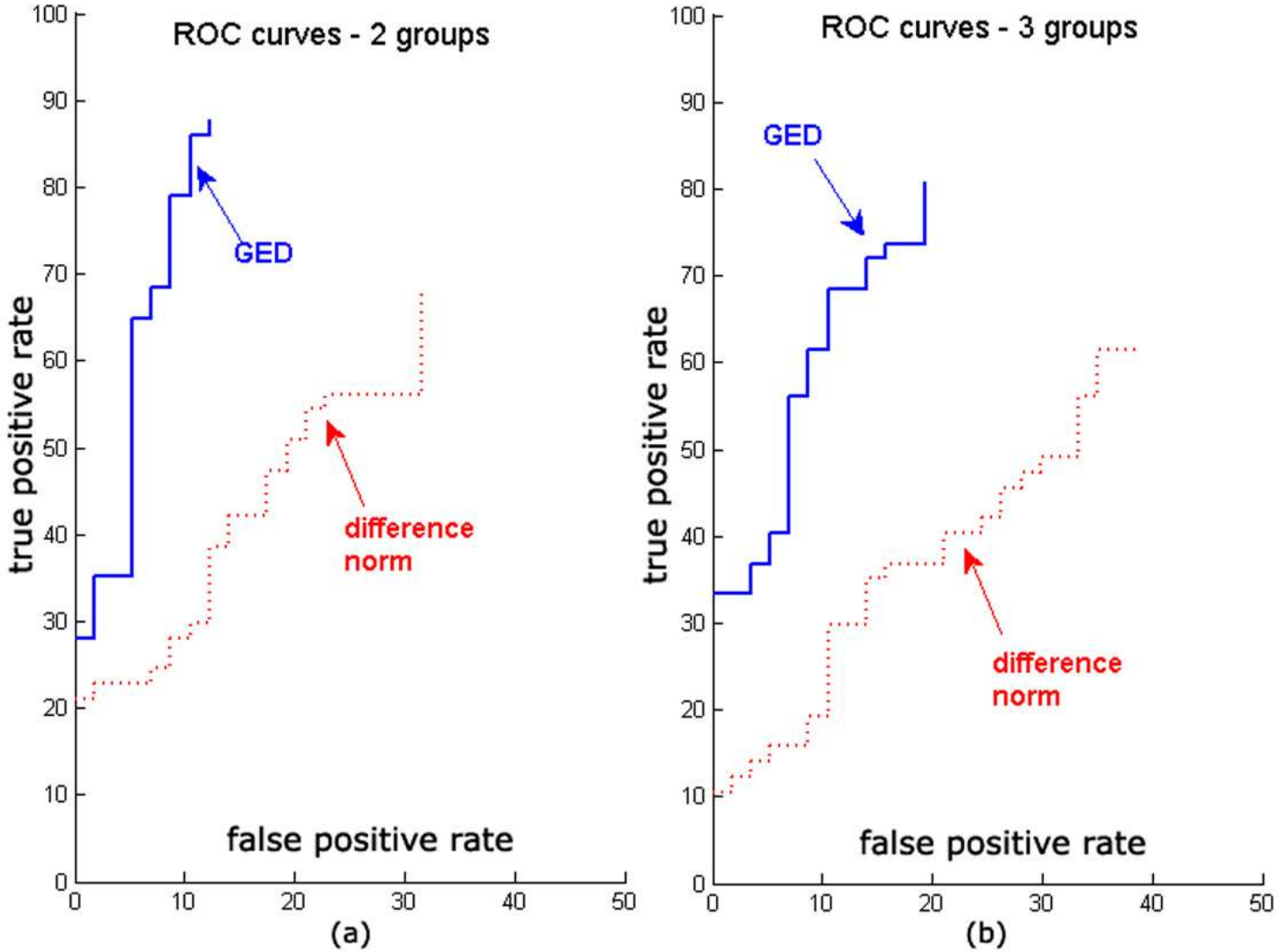
Summary of Classification algorithm



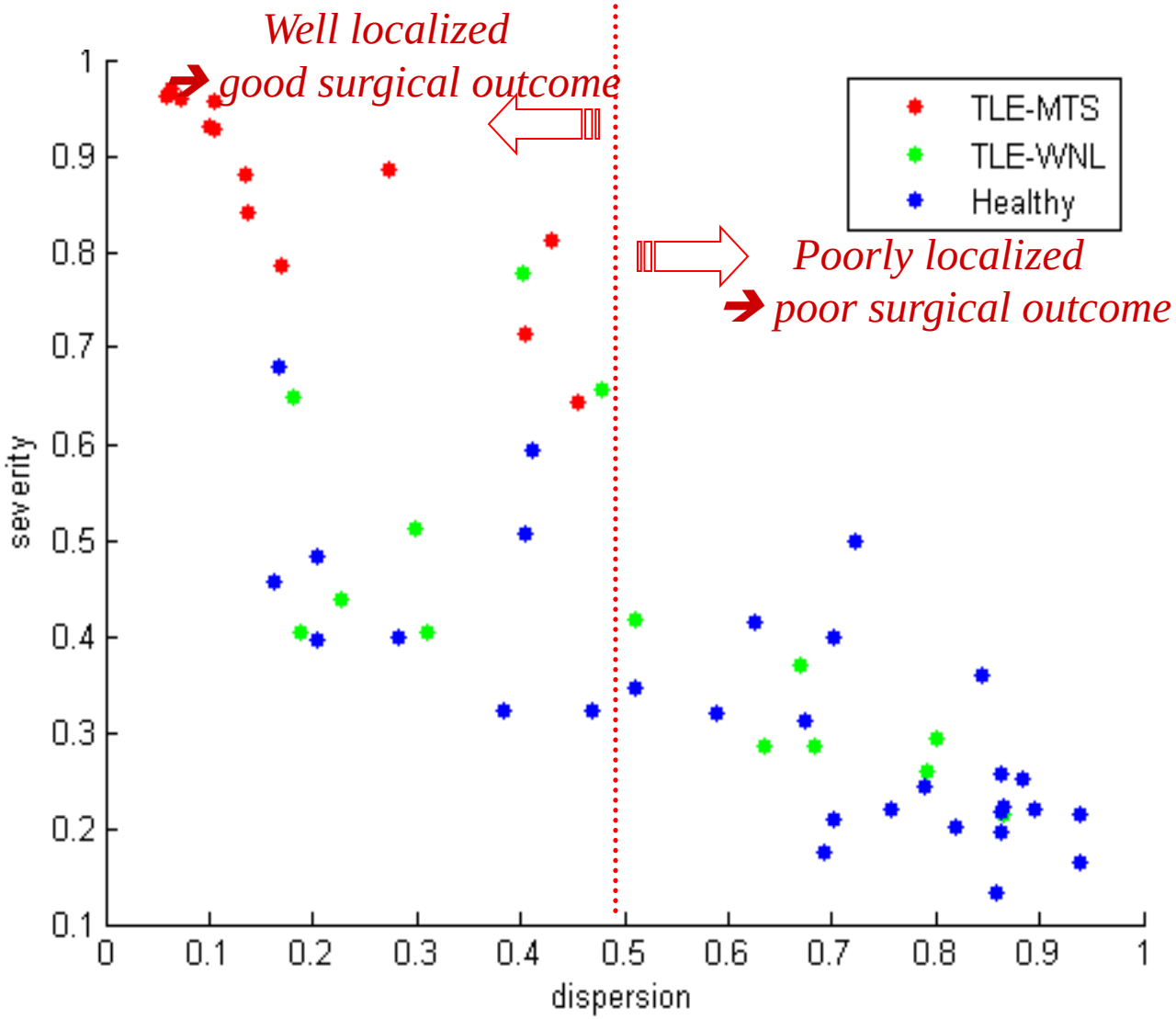
Classification of Epilepsy Networks



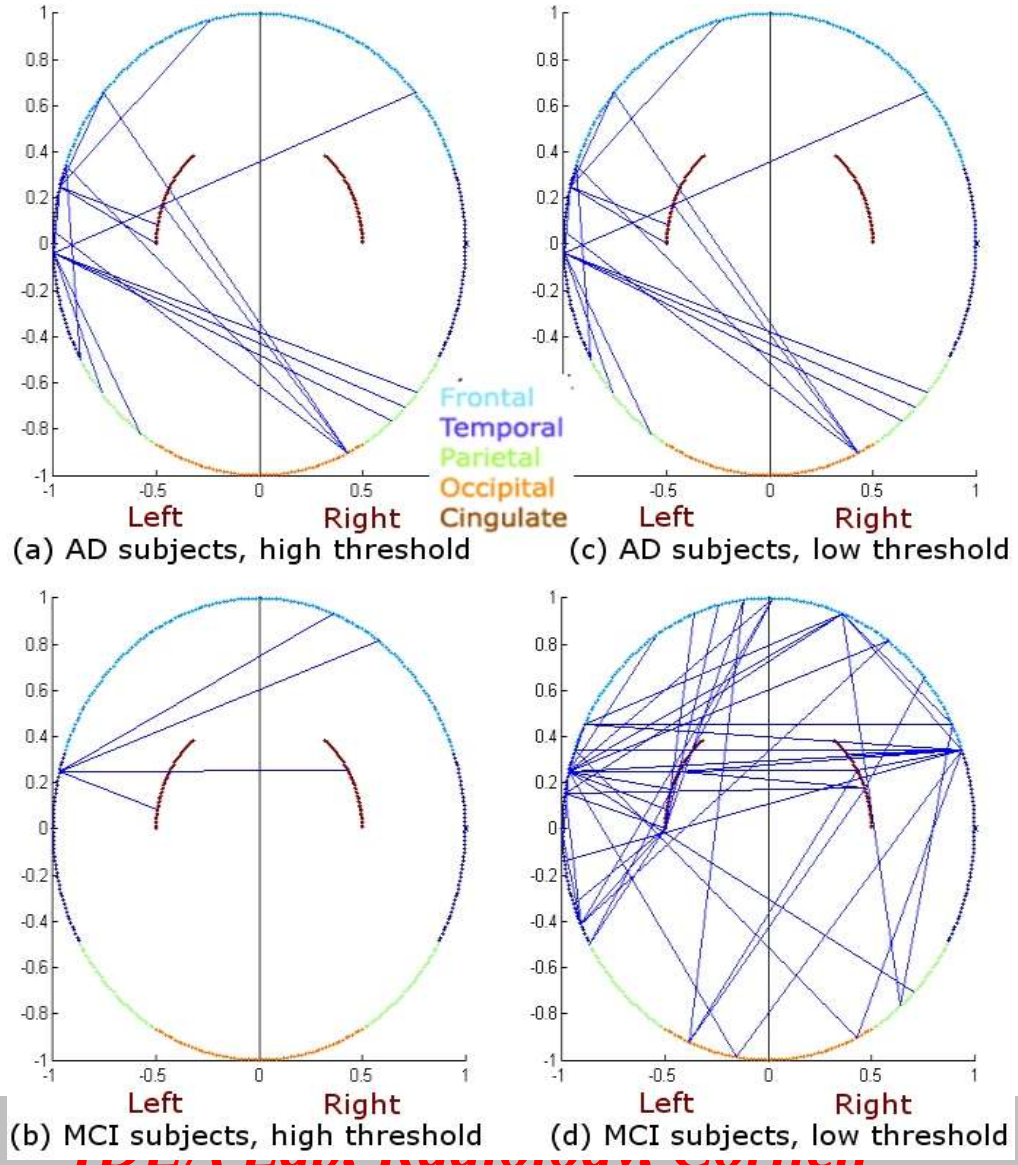
Epilepsy Network Classification – 2/3 Groups

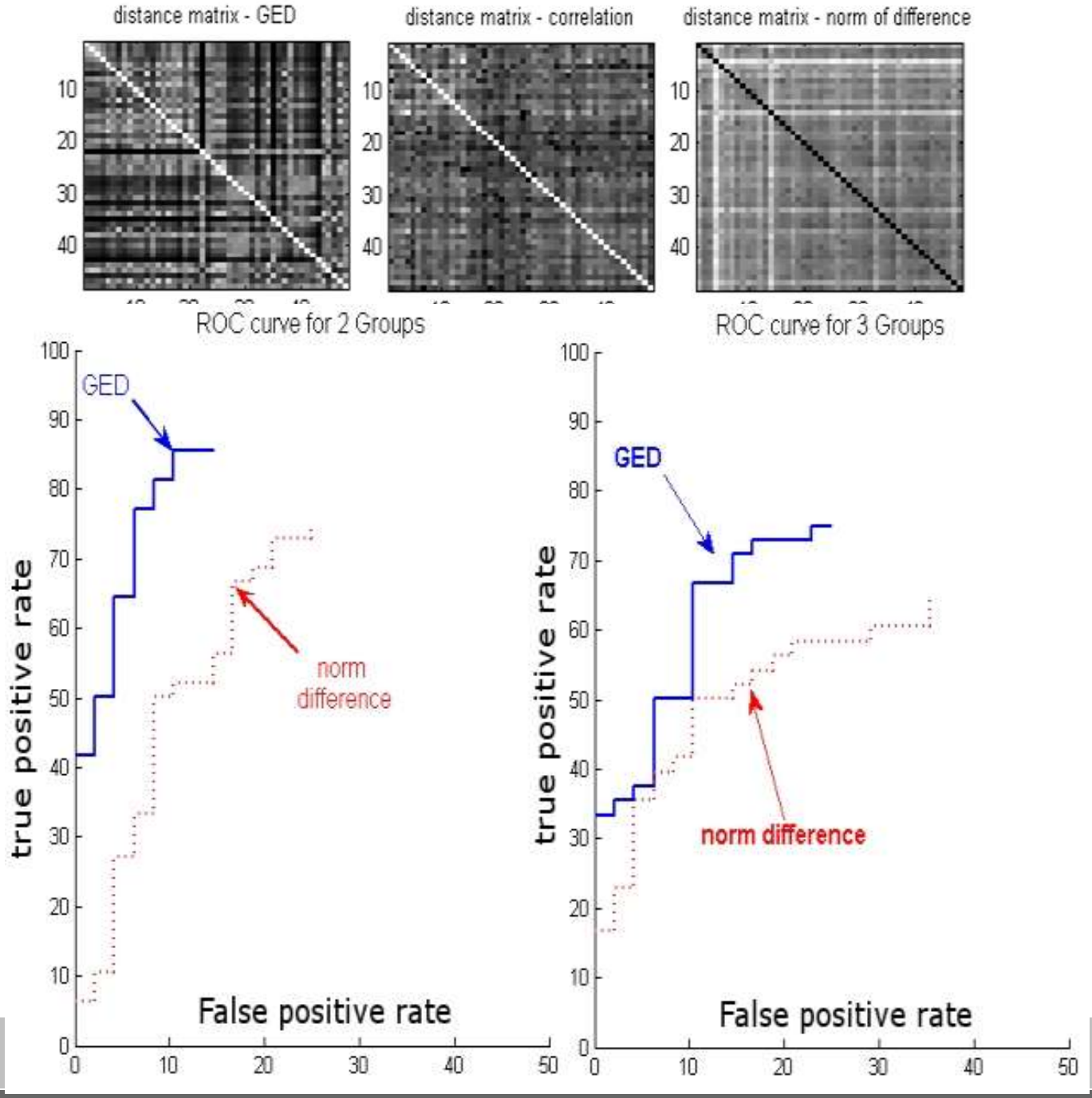


Dispersion and Severity



Classification of AD/MCI/Healthy




distance matrix - GED
distance matrix - correlation
distance matrix - norm of difference
ROC curve for 2 Groups
ROC curve for 3 Groups
GED
norm
difference
true positive rate
False positive rate
GED
norm difference
true positive rate
False positive rate

Introduction: Analysis of Data Derived from Medical Images

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